STEREOCHEMICAL AND MECHANISTIC STUDIES ON THE
ANIONIC OLIGOMERIZATION OF 2- AND 4-VINYLPYRIDINES

BY

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Major Department: Chemistry

In order to elucidate the mechanism of the anionic oligomeriza-
tion of 2-vinylpyridine, reactions of the 1,3-di(2-pyridyl)butane
anion lithium salt with 2-vinylpyridine as well as with other mono-
mers and electrophiles were investigated. With 2-vinylpyridine and
certain other monomers, the reaction proceeds in a non-stereoselec-
tive fashion, whereas 4-vinylpyridine and alkyl halides add with a
high degree of meso stereoselectivity. These results have been shown
to be consistent with coordination of the Li^+ counterion by the penul-
timate 2-pyridine nitrogen lone pair. Such a coordination would favor
the ion pair configuration which leads to preferred meso placement of
monomer or electrophile. The corresponding anionic oligomerization
of 4-vinylpyridine indicates that the lack of intramolecular coordina-
tion of Li^+ leads to random stereochemical placement of monomer and
methyl iodide.

x

Studies on the proton transfer equilibrium between alkali metal salts of 2-ethylpyridine and model dimers indicate large differences in the equilibrium constant K_{app} with the different alkali metal counterions. These are consistent with differences in intramolecular complexation, Li^+ being the most strongly complexed, followed by Na^+ and K^+. In addition, cryptation of the Li^+ counterion leads to a marked decrease in K_{app}. The temperature dependence of these equilibria indicates that the intramolecular coordination is favored partially due to entropic factors. Dimers with penultimate groups which are incapable of complexing the M^+, such as phenyl or 3-methyl-2-pyridyl, yield K_{app} values which approach unity in the equilibria. Nevertheless, these dimer anions are stabilized to a small extent, presumably due to some additional effect of the penultimate group.

Degradation reactions which occurred upon treatment of the 2-vinylpyridyl oligomers with 2-ethylpyridyl anions were also investigated. Such reactions were shown to be consistent with a mechanism in which an alkene was formed upon expulsion of an α-pyridyl carbanion. These observations confirm reports by other authors of a similar mechanism operating in the cleavage of poly-2-vinylpyridine chains in the presence of carbanions.

CHAPTER I

INTRODUCTION

In the past thirty years or so, there has been a great deal of interest in the stereoregular polymerization of vinyl monomers. This interest has been partly due to the new and important physical properties that stereoregular polymers may have, and partly due to the interesting fundamental phenomena controlling the mechanism of stereoregulation. Factors such as monomer structure, the nature of the initiator, solvent, and temperature all may play a role in determining the stereochemical composition of a polymer.

The anionic polymerization of 2- and 4-vinylpyridine provides a system for which a study of the stereoregulating mechanism would be of interest. For example, highly isotactic poly-2-vinylpyridine has been prepared by Grignard[1-4] and dialkylmagnesium[3,5] initiators, but under similar conditions 4-vinylpyridine gives only "atactic" polymers.[1,2,6] A study of the corresponding anionic oligomerization processes would provide a deeper understanding of the factors controlling stereoregulation. Furthermore, the carbanionic intermediates in vinylpyridine polymerization are very stable, and model compounds of these have been well studied. Therefore, the role of the carbanion centers in the oligomerization and polymerization may be more closely examined.

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The simplest models for the active centers in the anionic polymerization of 2-vinylpyridine are the alkali metal salts of 2-ethylpyridine. The lithium salt has been shown[7] by NMR measurements and CNDO/2 calculations to be sp^2 hybridized at C_α with a great deal of electron density delocalized into the pyridine ring. These studies also suggest that the lithium ion exists above the plane of the pyridine ring overlapping with the p orbitals of C_α and the nitrogen (Figure 1). Matsuzaki et al.[8] have found similar results for the position of the lithium ion for the cumyl anion. Because of the sp^2
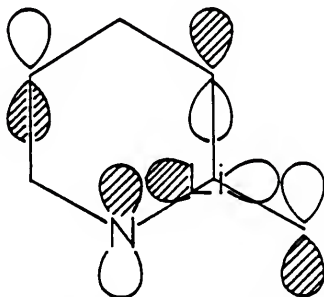
Figure 1. Overlap of Li p Orbital with the HOMO of the 2-Picolyl Anion.

hybridization and extensive delocalization into the ring, lithio-2-ethylpyridine may exist as both the E and Z isomers. Table 1 lists the results as determined by ^{1}H NMR[7,9] for the E:Z ratios as a function of metal ion. Coalescence of these isomers is not observed at temperatures up to 100°C, indicating that the equilibrium between E and Z anions is very slow on the NMR time scale. In the dimeric and

Table 1

E:Z Ratio in Lithio-2-Ethylpyridine as a Function of Counterion[a]

Counterion	Solvent	%E:%Z
Li	THF	95: 5
Na	THF	86:14
K	THF	80:20
Li	THF/TG[b]	66:34
Li	THF/[2.2.1]	36:64
Na	THF/TG[b]	66:34
K[c]	NH$_3$	45:55

[a] At 25°C

[b] TG = tetraglyme

[c] At -40°C; Private communication from J.A. Zoltewicz

trimeric model anions, the E:Z ratio is found to be 1:1 with both Li and K counterions.[10] This ratio is presumably the result of the mode of monomer presentation, which must be random with respect to the position of the nitrogen atom (Figure 2). Interestingly, monomer placement is selective with respect to β-carbon stereochemistry as shown by addition of E-β-deuterio-2-vinylpyridine.[9,11]

Conductance measurements[12-14] on living poly-2-vinylpyridine (Na$^+$ counterion) indicate that it has a dissociation constant about two orders of magnitude lower than living polystyrene (Na$^+$ counterion) in THF (Table 2), Moreover, living polystyrene capped with a single unit of 2-vinylpyridine is somewhat more dissociated than
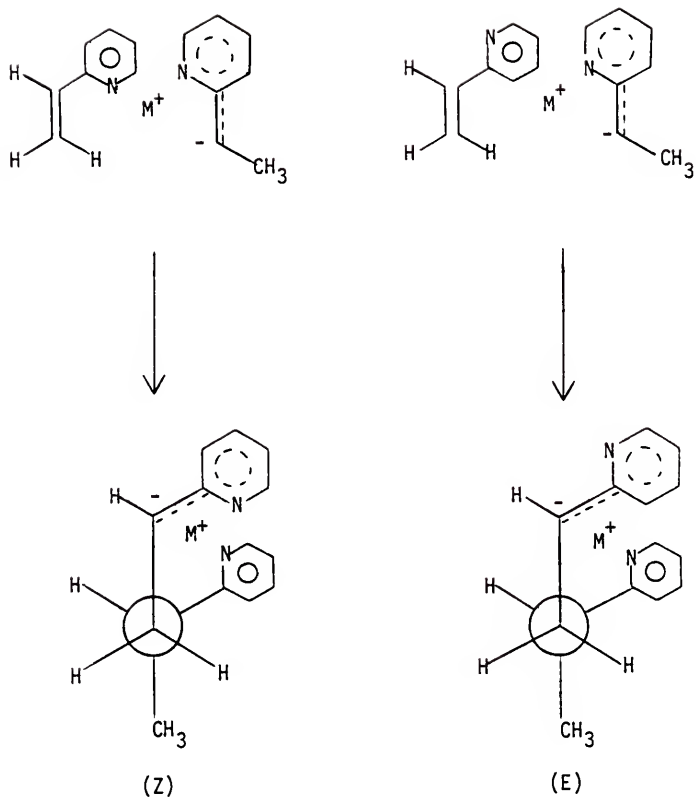
Figure 2.   Possible Modes of Monomer Presentation in the
Anionic Oligomerization of 2-Vinylpyridine.

Table 2

Dissociation Constants for Living Polymers in THF

	T (°C)	K_d
$P2VP^-,Na^+$	23	8.3×10^{-10} mol/l
$PSty^-,Na^+$	25	1.5×10^{-7} mol/l
$(PSty)-2VP^-,Na^+$	25	6.2×10^{-9} mol/l
$P4VP^-,Na^+$	23	5×10^{-9} mol/l
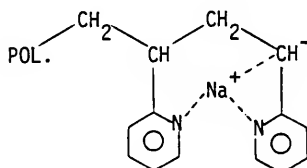
poly-2-vinylpyridine. Intramolecular coordination of the metal ion by the penultimate pyridine group has been invoked to explain the lower dissociation constant. The penultimate pyridine group "ties up" the metal ion, thus decreasing ion pair dissociation. With living polystyrene or polystyrene capped with a unit of 2-vinylpyridine, intramolecular coordination is not possible, and the ion pairs may be more readily dissociated. Intramolecular coordination of the metal ion has also been proposed in the active centers of poly(methyl methacrylate).[15,16]

Previous studies on the anionic oligomerization of 2-vinylpyridine[11,17-20] (Equation 1) have indicated that the high methylation stereoselectivity of the lithium salt of dimer [3] is consistent with

$$\underset{\overset{|}{R}}{CH_3CH_2} \xrightarrow[\substack{THF \\ -78°C}]{n-BuLi} \underset{\overset{|}{R}}{CH_3CH^-,Li^+} \xrightarrow{\overset{R}{\diagup}}$$

$$[\underline{1}] \qquad\qquad\qquad [\underline{2}]$$

(1)

$$\underset{\overset{|}{R}\;\;\overset{|}{R}}{CH_3 {-}(CHCH_2{)}_{\overline{n}}CH^-},Li^+ \xrightarrow{CH_3I} \underset{\overset{|}{R}\;\;\overset{|}{R}}{CH_3{-}(CHCH_2{)}_{\overline{n}}CHCH_3}$$

$$[\underline{3}] - [\underline{5}] \qquad\qquad\qquad [\underline{6}] - [\underline{8}]$$
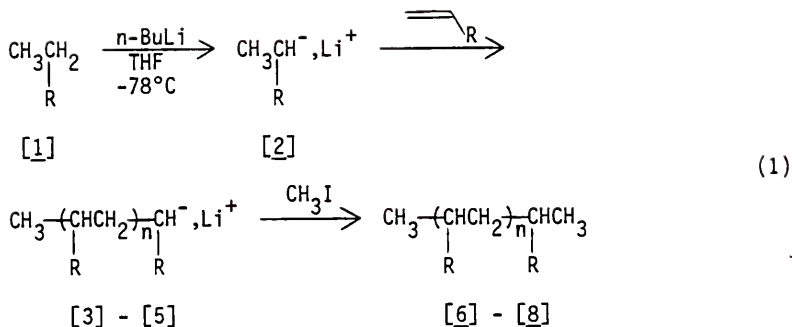
R = 2-pyridyl; [$\underline{3}$], [$\underline{6}$] n = 1; [$\underline{4}$], [$\underline{7}$] n = 2; [$\underline{5}$], [$\underline{8}$] n = 3

intramolecular coordination of the metal ion by the penultimate pyri-
dine group. When the oligomerization is initiated by other alkali
metal salts of 2-ethylpyridine, the stereoselectivity of methylation
decreases with increasing cation radius (Table 3). The addition of

Table 3

Methylation Stereochemistry[a] of Anion [$\underline{3}$][b] as a
Function of Cation and Solvent or Coordinating Agent

Cation	Solvent/Coordinating Agent	% Meso	Reference
Li	THF	>99	21
Na	THF	~99	21
K	THF	85	21
Rb	THF	76	21
Li	THF/[2.1.1]	65	22
Na	THF/[2.2.2]	58	22
Na	THF/18-crown-6	58	22

[a] At -78°C
[b] ~10^{-2} M

cation solvating agents such as crown ether or cryptand also results in a loss of methylation stereoselectivity. Moreover, methylation of the corresponding 4-vinylpyridyl dimer anion results in an approximately 50:50 mixture of meso and racemic products.[17] Clearly, upon disruption of the intramolecular coordination, methylation occurs in a relatively non-stereoselective fashion.

The high meso stereoselectivity has been attributed to the predominance of ion pair diastereomer [9] over [10] (Figure 3). Examination of models of these diastereomeric ion pairs indicates that [9a] will be favored over [10a] because of butane-gauche interactions between the CH_3 group and the CH_2C^- bond as well as non-bonded interactions between the CH_3 group and the ion pair. Rotation of the CH_2-CH-R bond by 180° followed by inversion of the carbanion pair leads to structure [10b] which would seem less likely since the metal ion is further removed from the penultimate group. Additional steric interactions are seen in [10a] with the methyl group interacting with the ultimate pyridyl group and the solvation shell of the counterion. Thus, the overall free energy of [9] may be several kilocalories lower than [10] and would result in a large predominance of [9]. Alkylation of [9] from the cation side leads to the observed meso product. Cation side attack is assumed since attack from the opposite side would result in a product separated ion pair (Figure 4). Such an ion pair is expected to be quite unfavorable.

Further support for the intramolecular coordination is provided by the lack of methylation stereoselectivity of dimer anion [11] (Table 4).[23] Methyl substitution at the 3'-position of the

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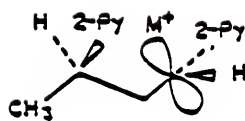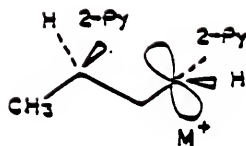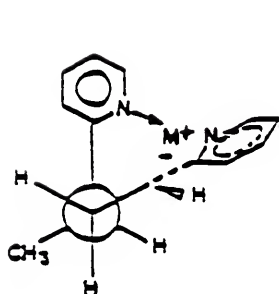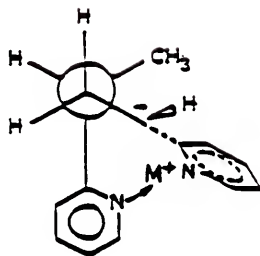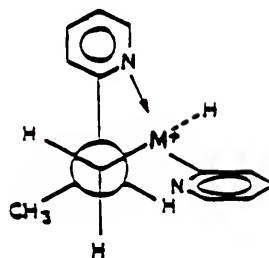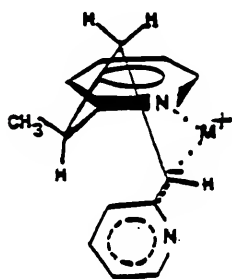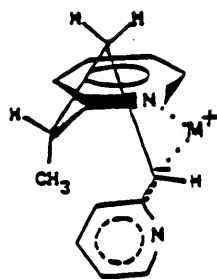
Figure 3. Diastereomeric Ion Pairs [9] and [10] and the Role of Intramolecular Coordination.
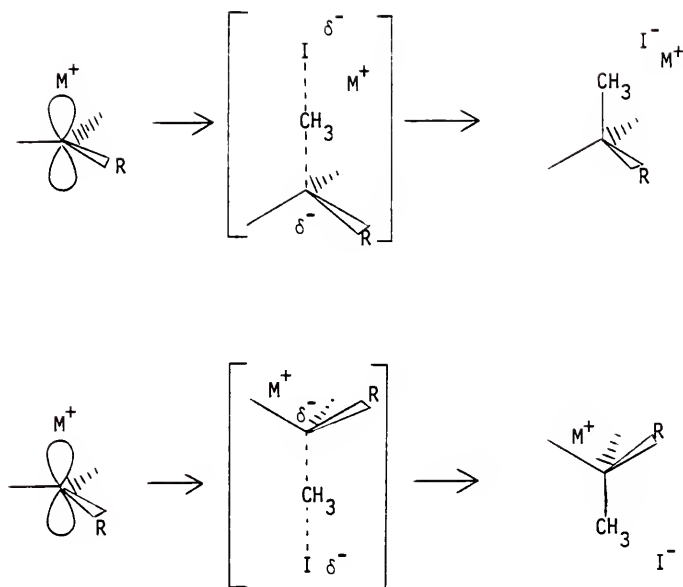
Figure 4. Cation Side vs. Opposite Side Attack of Methyl
Iodide on a Carbanion.

$CH_3CH-CH_2CH^-$, Li^+
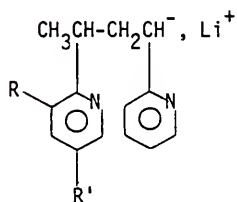
[11] R = CH_3, R' = H
[12] R = H, R' = CH_3

Table 4

Stereochemistry of Methylation of Dimer Anions [11], [12] and [3][a]

Dimer Anion	% (R,S or S,R) meso-like	% (R,R or S,S) racemic-like
[11]	24	76
[12]	99	1
[3]	>99	<1

[a]Determined by capillary GC.

penultimate pyridine ring decreases the stereoselectivity of methyla-
tion with respect to unsubstituted dimer, while substitution at the
electronically equivalent 5'-position does not significantly lower
methylation stereoselectivity. This indicates that steric interac-
tions between the 3'-methyl group and the methyl and methylene groups
of the chain disrupt the intramolecular coordination in [11].
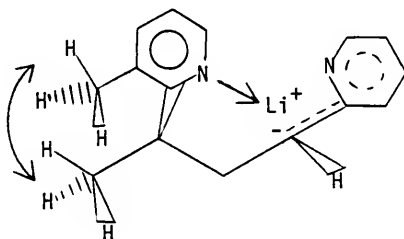
In contrast to the high meso-stereoselectivity of methylation,
2-vinylpyridine adds to [3] in a rather non-selective fashion (60%
meso, 40% racemic).[20] The reason for this large difference in

stereoselectivity (>99/1 vs. 1.5/1) is not very well understood. Effects such as steric bulk or electronic factors may play a role in the stereochemistry of 2-vinylpyridine addition. This unsolved problem is crucial to understanding the mechanism of anionic polymerization of 2-vinylpyridine.

Research Objectives

The purpose of this study may be summarized as follows:

A. To further our understanding of the stereoselective methylation of 2-vinylpyridine oligomer anions. Specifically, to determine to what extent the intramolecularly complexed form of the carbanionic intermediates exists. This is accomplished by examination of the equilibrium between alkali metal salts of 2-ethylpyridine and oligomeric model compounds.

B. To determine why the methylation of 2-vinylpyridine oligomer anions is stereoselective while the addition of 2-vinylpyridine is not. A systematic study of the reaction of these carbanions with various electrophiles and monomers is used to point up some of the factors important in controlling the stereochemistry of these reactions.

C. To elucidate the stereochemistry of the anionic oligomerization of 4-vinylpyridine.

D. To understand degradation reactions which occur when poly-2-vinylpyridine is treated with carbanions. Oligomers of 2-vinylpyridine are used as model compounds to determine the products formed in these degradation reactions.

CHAPTER II

EXPERIMENTAL

Since the presence of trace amounts of electrophilic impurities will affect anionic active centers, all reagents were carefully purified and transferred in vacuo, and all reactions were carried out in Pyrex glass vessels under high vacuum (10^{-5} mm to 10^{-6} mm Hg). All stopcocks and ground glass connections were lubricated with Dow Dorning high vacuum silicone grease. Transfer of reagents was performed by distillation in vacuo or through glass breakseals which may be broken by striking with magnetic rods sealed in glass.

Purification of Reactants

In all reactions, tetrahydrofuran (THF) was used as the solvent. THF was refluxed over Na/K alloy for several hours, then distilled onto fresh Na/K alloy. A small amount of benzophenone (1 gram per liter of THF) was added as an indicator. The deep purple color of the benzophenone dianion indicated the absence of traces of water, oxygen, or other impurities.

All reactants were liquids at room temperature and were purified by stirring over CaH_2 for at least 8 hours and degassed in vacuo followed by distillation onto fresh CaH_2 and stirring for at least another 8 hours. The liquid was then distilled in vacuo into an ampule equipped with a breakseal and sealed off. If the material as

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purchased was particularly impure, a fractional distillation was performed before drying over CaH_2 and distillation in vacuo. Methyl iodide and ethyl iodide were stirred over CaH_2 and distilled in vacuo onto fresh CaH_2 in a vessel equipped with a vacuum stopcock and ground glass joint for repeated use on the vacuum line. Liquids with high boiling points were stirred over CaH_2 and degassed in vacuo followed by filtration through sintered glass filters into ampules and sealed off.

Lithium tetraphenyl boron prepared by the method of Szwarc et al.[24] was recrystallized from 1,2-dichloroethane and dried overnight in vacuo. The dried solid was dissolved in THF and the solution transferred in vacuo to an ampule equipped with a breakseal and sealed off.

Preparation of Ethylpyridyl Alkali Metal Salts

Lithio-2-ethylpyridine

A solution of n-butyllithium (Aldrich) in hexane was introduced into a 250 ml round bottom flask with a clean, dry syringe. The apparatus (Figure 5) was then sealed off and evacuated, removing the hexane into a liquid nitrogen trap. THF was distilled into the flask at -78°C, followed by introduction of one equivalent of 2-ethylpyridine with respect to n-butyllithium through a breakseal upon which the solution immediately turned bright red. The solution was then warmed up and kept at room temperature for at least 30 minutes, while butane was removed periodically by opening the apparatus to the vacuum. The apparatus was sealed from the vacuum line and the solution poured into a side arm flask and sealed from the main flask.
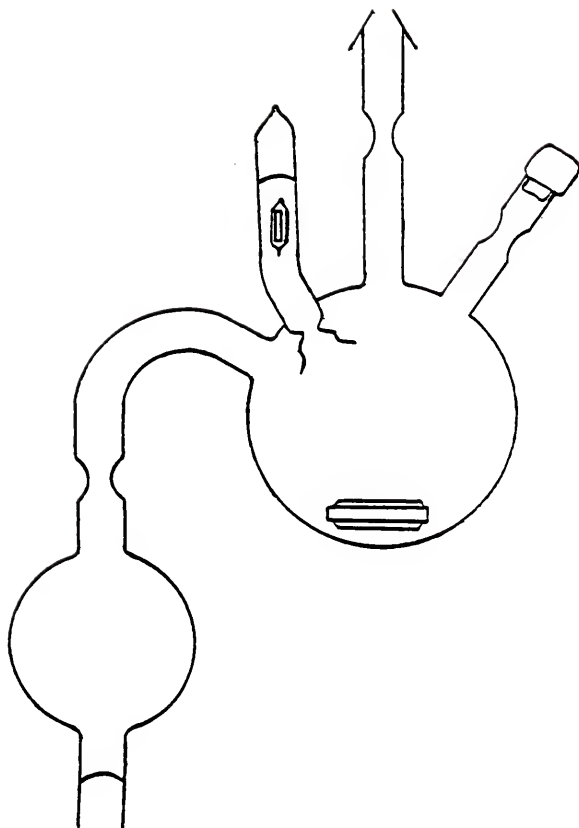
Figure 5. Apparatus for the Preparation of Alkali Metal 2-Ethylpyridyl Salts.

The lithio-2-ethylpyridine (2EPLi) was purified by recrystalliza-tion in the apparatus shown in Figure 6. The crude 2EPLi solution was introduced into the main flask (A), and the THF was removed by distil-lation on the vacuum line until only a small amount (~10 cc) of sol-vent remained. Approximately 40 cc of n-hexane (dried 24 hours over Na/K alloy) was then distilled onto the viscous 2EPLi residue until all the salt dissolved. The apparatus was sealed off and kept in a freezer at -20°C until crystallization occurred. Solvent was then de-canted from the 2EPLi crystals into a side arm flask (B), and the crystals were washed with hexane which was distilled back from the side arm flask. After several washings, the side arm (B) was sealed off and the crystals dissolved in THF freshly distilled into the ap-paratus. The THF/2EPLi solution was poured into a second side arm (C) (equipped with a breakseal) and sealed. Purity of the 2EPLi was checked by isolating a small portion of the solution and terminating this portion with CH_3I and the absence of impurities verified by gas chromatography. The concentration of 2EPLi in THF was determined by terminating a portion of the solution with CH_3I and titrating the LiI by the method of Vollhard.[25] Alternatively, the solution was termi-nated with H_2O and titrated for the total base concentration with standard HCl solution to pH $\cong$ 7 using bromthymol blue as indicator. The total base concentration reflected the presence of one equivalent of 2-ethylpyridine and one equivalent of hydroxide ion. Thus, the concentration of 2EPLi in solution was equal to half the total base concentration.

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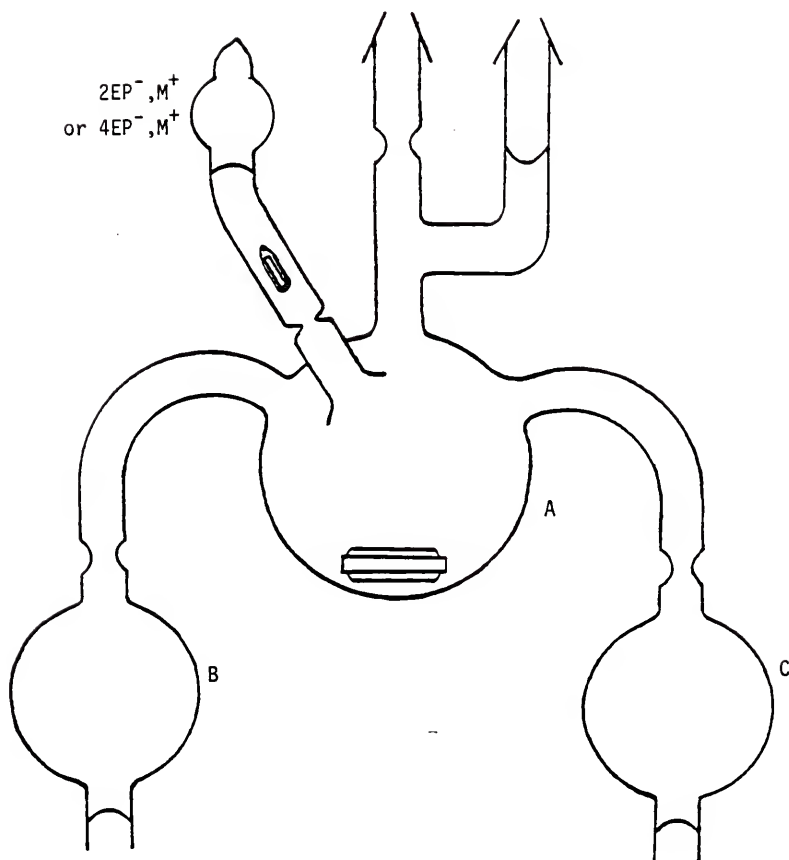
Figure 6. Apparatus for the Recrystallization of Alkali Metal
Ethylpyridyl Salts.

Sodio- and Potassio-2-ethylpyridine

A sodium (or potassium) mirror was prepared in an evacuated 300 ml round bottom flask (Figure 7) by vacuum coating the walls of the flask with the metal vapor produced by heating a reservoir (A) containing the metal with a gentle flame. After forming the mirror, the reservoir was sealed off, and THF (150 ml) was distilled into the flask through the vacuum line. α-Methylstyrene was then added from a breakseal at room temperature. A red color developed almost immediately upon addition. After reaction of the metal with α-methylstyrene was complete (~1 hour), the dark red α-methylstyrene oligomer dianion solution was poured into a side arm flask (B) and sealed from the main flask. The flask containing the dianion solution was cooled to -78°C to polymerize any excess α-methylstyrene. After 1 hour, a slight excess of 2-ethylpyridine was added at -78°C.

The purification and titration procedures for sodio-2-ethylpyridine (Na2EP) and potassio-2-ethylpyridine (K2EP) were identical to those for Li2EP.

Lithio-4-ethylpyridine

Attempts to prepare lithio-4-ethylpyridine (4EPLi) by addition of 4-ethylpyridine to n-butyllithium in THF at -78°C failed to give the desired carbanion. After termination with CH_3I, 2-butyl-4-ethyl-5-methylpyridine was produced almost quantitatively.
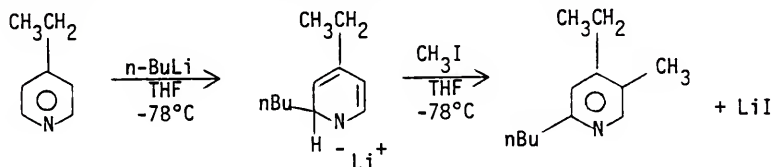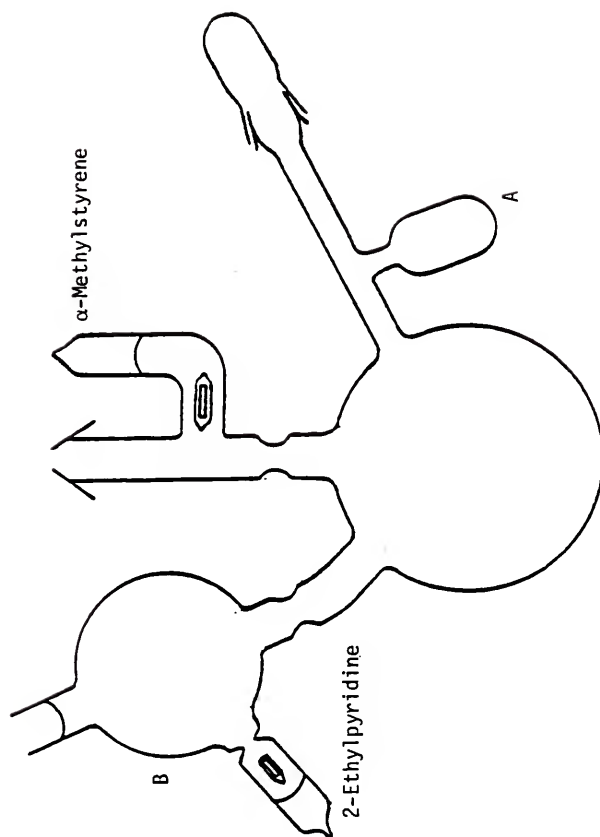
Figure 7. Apparatus for the Preparation of Sodio- and Potassio-2-Ethylpyridyl Salts.

To avoid this reaction, 2,4-diphenyl-4-methyl-2-nonyllithium (DMNL) was used to deprotonate 4-ethylpyridine. In an apparatus similar to that used for the preparation of lithio-2-ethylpyridine (Figure 5), 2 equivalents of α-methylstyrene were added to 1 equivalent of n-butyllithium in THF at 0°C. The solution was reacted for 15 minutes, then cooled to -78°C for 15 minutes to polymerize any excess α-methylstyrene. One equivalent of 4-ethylpyridine was then added directly at -78°C and allowed to react at room temperature for 30 minutes, the color of the solution changing from deep red to light orange. The solution was transferred to a side arm flask equipped with a break-seal and sealed off. The crude lithio-4-ethylpyridine was purified by recrystallization in a manner identical to that for lithio-2-ethylpyridine.

Oligomerizations

2-Vinylpyridyl Oligomers

Purified lithio-2-ethylpyridine in THF was introduced through a breakseal into an evacuated 250 ml round bottom flask (Figure 8), and 125-150 ml of THF was distilled into the flask at -78°C. The experiments were generally run with a carbanion concentration of about 5 x 10^{-2} M. 2-Vinylpyridine (1.5-2.0 equivalents) was distilled slowly over a 1-2 hour period from a 25 ml round bottom flask attached to the main flask, which was kept at -78°C. After monomer addition was complete, the anions were terminated with various reagents. In the case of termination with methanol, methyl halides, or ethyl iodide, the purified terminating agent was distilled through the vacuum line onto the oligomer anion solution. For termination with other reagents

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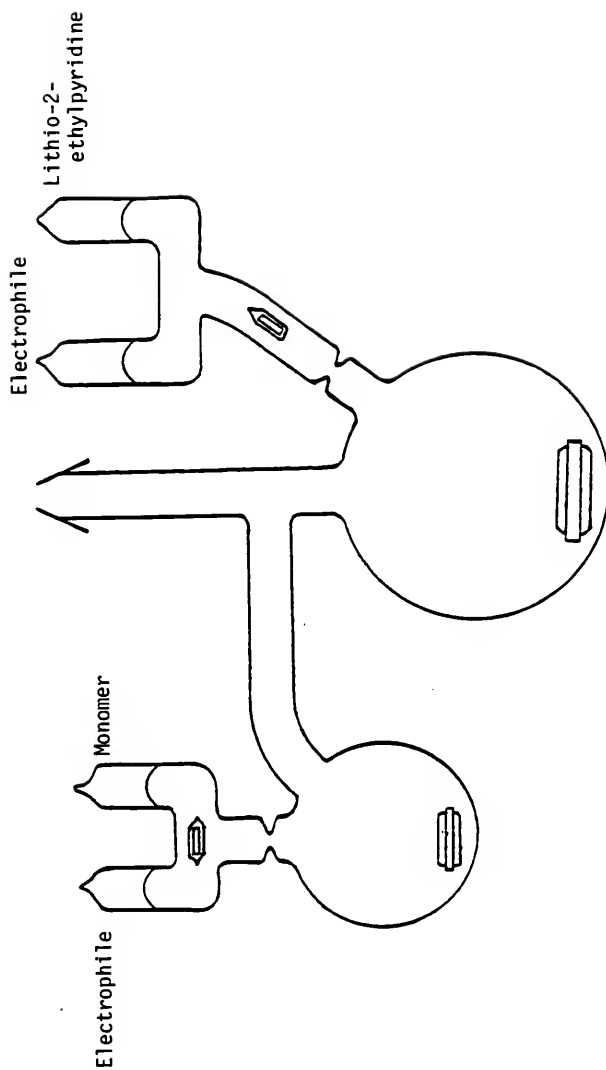
Figure 8. Apparatus for Oligomerization of Vinylpyridine Monomers.

which are relatively easily distilled in vacuo (i.e., trimethylsilyl chloride, 4-vinylpyridine, acetone-d_6, isopropyl bromide), the terminating agent was distilled onto the carbanion from the same side arm flask as the 2-vinylpyridine monomer. For reaction of the oligomer anions with electrophiles which will not vacuum distill easily (i.e., benzyl chloride, benzhydryl chloride, 1,1-diphenylethylene, benzaldehyde), the electrophile was added directly to the carbanion solution through a breakseal attached to the reaction flask. Electrophilic reagents which, upon addition, form new anionic species were subsequently protonated with methanol distilled through the vacuum line. All reactions were carried out at -78°C. However, the more hindered electrophiles, such as isopropyl bromide and benzhydryl chloride, react very slowly at -78°C, and the solutions were allowed to warm up to about -40°C in order to ensure complete reaction.

After reaction, the volatile fraction was removed by evacuation on the vacuum line. The apparatus was then removed from the line, and the residue was dissolved in 125 ml of 10% HCl. The HCl solution was washed several times with methylene chloride, then neutralized with Na_2CO_3. The aqueous solution was extracted with 300 ml of methylene chloride and the organic layer dried over anhydrous Na_2SO_4 overnight. Finally, the dried methylene chloride solution was evaporated in a rotary evaporator. The yield of oligomers was 30-80%, depending on the monomer/initiator ratio and the rate of monomer addition. High [M]/[I] ratios and fast rates of monomer addition led to an increased formation of polymer, which was the major by-product. Preparative liquid chromatography was used to separate the crude product mixture into the various oligomer fractions.

4-Vinylpyridine Oligomers

The preparation of 4-vinylpyridine oligomers was essentially identical to the preparation of 2-vinylpyridine oligomers, using re-crystallized 4-ethylpyridyllithium as initiator and 4-vinylpyridine as monomer. Termination was made with either methanol or methyl iodide. Isolation of the various oligomers was carried out by preparative liquid chromatography.

Epimerization Studies

Partial epimerization of isotactic 4-vinylpyridine tetramer obtained by liquid chromatography was studied to assign the stereoisomer peaks in gas chromatography. Samples (~50 mg) were dried in vacuo in vessels equipped with ground glass joints. Potassium tert-butoxide (0.09 g in 1.0 ml tBuOH), prepared by reaction of K metal with tBuOH, was added to the sample under argon atmosphere with a clean, dry syringe. The vessels were then capped with rubber septum stoppers. Aliquots of the solution (~100 μl) were taken at specified intervals, neutralized with H_2O, and analyzed by capillary column gas chromatography.

Equilibrium Studies

Preparation of 1,3-Di(2-pyridyl)butane

This product was obtained by vacuum distillation of the crude mixture of protonated 2-vinylpyridyl oligomers; b.p. 125-127°C (0.1 mm Hg). ^{1}H NMR 1.26 ppm, doublet, J = 6.7 Hz, (3H); 2.05 ppm, multiplet, (2H); 2.83 ppm, multiplet, (3H); 7.30 ppm, multiplet, (6H); 8.40 ppm, multiplet, (2H).

Preparation of 2,4-Di(2-pyridyl)pentane

This product was also obtained by vacuum distillation of the crude mixture of methylated 2-vinylpyridine oligomers; b.p. 106-108°C (0.25 mm Hg). ^{1}H NMR 1.31 ppm, doublet, J = 6.5 Hz, (6H); 2.10 ppm, multi-plet, (2H); 2.80 ppm, multiplet, (2H); 7.30 ppm, multiplet, (6H); 8.40 ppm, multiplet, (2H).

Preparation of 2-Ethyl-3-methylpyridine

2,3-Lutidine (9.3 g, ICN K&K Laboratories) in 150 ml THF was treated with one equivalent of n-butyllithium in vacuo at -78°C. The carbanion precipitated at -78°C, so the solution was warmed to about -50°C and terminated with methyl iodide. Excess methyl iodide and the solvent were removed by evaporation on a rotary evaporator, and the residue was dissolved in 100 ml of methylene chloride. The solu-tion was washed twice with 100 ml of water and dried over Na_2SO_4 over-night. After removal of the solvent, the crude product, analyzed by ^{1}H NMR and gas chromatography, was shown to be about 90% 2-ethyl-3-methylpyridine. The product was purified by fractional distillation; b.p. 178-180°C. ^{1}H NMR 1.43 ppm, triplet, J = 7.5 Hz, (3H); 2.17 ppm, singlet, (3H); 2.74 ppm, quartet, J = 7.5 Hz, (2H); 7.12 ppm, multiplet, (2H); 8.30 ppm, multiplet, (1H).

Preparation of 1-(2-Pyridyl)-3-(3-methyl-2-pyridyl) butane

In an evacuated oligomerization apparatus (Figure 8), one equiv-alent of 2-ethyl-3-methylpyridine was added to 1.1 equivalents of n-butyllithium in THF at -78°C. The characteristic orange color of the 2-ethyl-3-methylpyridyl anion formed immediately. The solution was warmed up to room temperature and allowed to react for 30 minutes,

then was cooled to -78°C followed by in vacuo distillation of one equivalent of 2-vinylpyridine. After monomer addition was complete, the anion solution was protonated with deaerated methanol distilled through the vacuum line. The crude product was extracted in the same fashion as the 2-pyridyl oligomer crude product, and the 1-(2-pyridyl)-3-(3-methyl-2-pyridyl) butane was isolated by preparative liquid chromatography. ^{1}H NMR 1.26 ppm, doublet, J = 7.0 Hz, (3H); 2.12 ppm, singlet, (3H); 2.15 ppm, multiplet, (2H); 2.80 ppm, multiplet, (3H); 7.20 ppm, multiplet, (5H); 8.47 ppm, multiplet, (2H).

Preparation of 1-(2-Pyridyl)-3-phenylbutane

2-Picoline (4.0 g, Aldrich) in 150 ml THF was treated with one equivalent of n-butyllithium in vacuo at -78°C. The resultant 2-picolyllithium was then reacted with 9.7 g of β-bromo-isopropylbenzene (Aldrich) at room temperature for 3 hours. The color changed from deep red to light yellow, indicating the 2-picolyllithium had reacted completely. The volatile fraction was then removed by evacuation into a liquid nitrogen trap on the vacuum line, and the remaining residue was dissolved in 125 ml of 10% HCl. The HCl solution was washed several times with methylene chloride, then neutralized with Na_2CO_3. The aqueous solution was extracted with 400 ml of methylene chloride and the organic layer dried over anhydrous Na_2SO_4 overnight. After removal of the methylene chloride on a rotary evaporator, the product was isolated (3.8 g, 41% yield) by vacuum distillation; b.p. 107-110°C (0.15 mm Hg). ^{1}H NMR 1.15 ppm, doublet, J = 6.5 Hz, (3H); 1.90 ppm, multiplet, (2H); 2.58 ppm, multiplet, (3H); 7.05 ppm, multiplet, (8H); 8.33 ppm, multiplet, (1H).

Preparation of 3-Methyl-1,3-di(2-pyridyl) butane

This product was prepared in a manner similar to that used for 2-vinylpyridyl oligomers, using lithio-2-methylpyridine as initiator and 2-(2-pyridyl) propene as the monomer. The reaction was terminated by distilling methyl iodide into the carbanion solution through the vacuum line. After work-up, the dimer was isolated from the crude product by preparative liquid chromatography. ^{1}H NMR 1.46 ppm, singlet, (6H); 2.35 ppm, multiplet, (4H); 7.37 ppm, multiplet, (6H); 8.58 ppm, multiplet, (2H).

General Procedure for Carbanion Equilibrium Reactions

In an evacuated 100 ml round bottom flask (Figure 9), 200 mg of the desired dimer [1,3-di(2-pyridyl)-butane, 1-(2-pyridyl)-3-(3-methyl-2-pyridyl)-butane, 2,4-di(2-pyridyl)-pentane, 3-methyl-1,3-di-(2-pyridyl)-butane, or 1-(2-pyridyl)-3-phenylbutane] were added to one

$$CH_3CH^-M^+ + CH_3CHCH_2CH_2 \underset{\longleftarrow}{\overset{K}{\longrightarrow}} CH_3CH_2 + CH_3CHCH_2CH^-M^+ \quad (2)$$
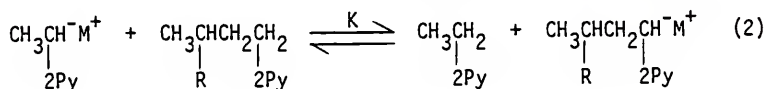
$$\underset{2Py}{} \quad \underset{R \quad 2Py}{} \quad \underset{2Py}{} \quad \underset{R \quad 2Py}{}$$

R = 2-pyridyl, phenyl, 3-methyl-2-pyridyl

2Py = 2-pyridyl

$$CH_3CH^-,M^+ + CH_3-CCH_2CH_2 \underset{\longleftarrow}{\overset{K}{\longrightarrow}} CH_3CH_2 + CH_3-C-CH_2CH^-,M^+$$

$$\underset{2Py}{} \quad \underset{2Py \ 2Py}{\overset{CH_3}{}} \quad \underset{2Py}{} \quad \underset{2Py \ 2Py}{\overset{CH_3}{}}$$
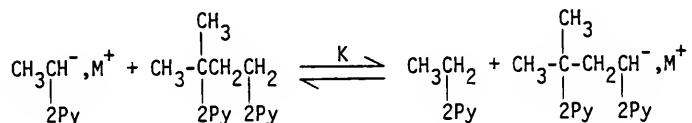
equivalent of an alkali metal 2-ethylpyridine salt in 15-20 ml of THF at room temperature. The solution was transferred to a side arm flask, divided, and each sample was brought to the desired tempera-ture and allowed to react. After a certain time interval, each sample
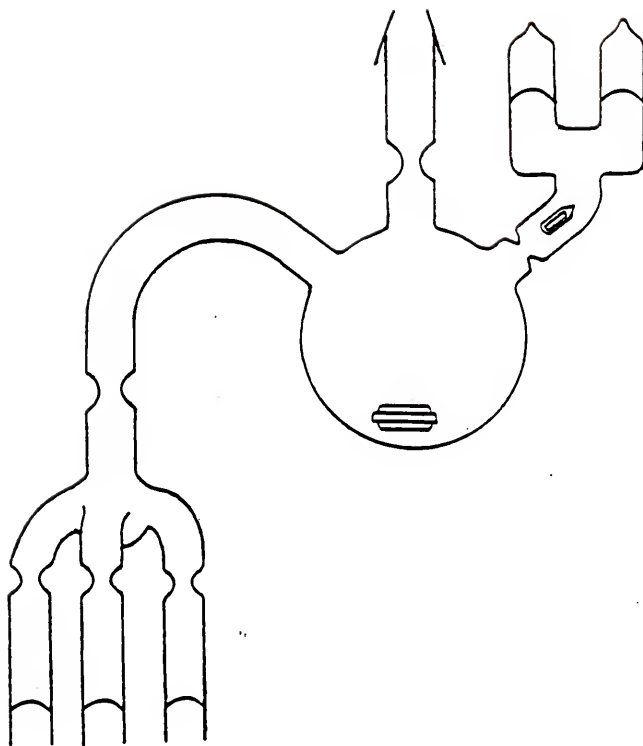
Figure 9. Apparatus for Carbanion Equilibrium Studies.

was connected to the vacuum line and terminated with ethyl iodide dis-
tilled in vacuo. The terminated mixtures were dissolved in methylene
chloride and washed several times with water. The organic phase was
then analyzed by capillary column gas chromatography.

When complexing agents (18-crown-6, [2.1.1] or [2.2.1] cryptands)
were used, the ethylpyridyl salt was allowed to react with the com-
plexing agent for 1-2 minutes at room temperature before addition of
the dimer to allow for complete cation complexation.

Determination of Equilibrium Constants

The apparent equilibrium constants in Equation 4 (p. 72) are
given by

$$K_{app} = \frac{[CH_3CH_2(2Py)][CH_3CHRCH_2CH(2Py)^-,M^+]}{[CH_3CH(2Py)^-,M^+][CH_3CHRCH_2CH_2(2Py)]}$$

upon termination with ethyl iodide. The ratios $[CH_3CH_2(2Py)]/[CH_3CH(2Py)^-,M^+]$ and $[CH_3CHRCH_2CH(2Py)^-,M^+]/[CH_3CHRCH_2CH_2(2Py)]$ may be
determined directly from the integrated areas of the GC traces of the
ethylated products. The apparent equilibrium constants are reported
as the product of these two ratios as measured on the gas chromatography.

Degradation Reaction Studies

Preparation of 1,3,5-Tri-(2-pyridyl)-hexane and 1,3,5,7-Tetra-(2-pyridyl)-octane

These products were isolated by preparative liquid chromatography
of the crude mixture of 2-vinylpyridyl oligomers.

General Procedure for Degradation Reaction Studies

The procedure was essentially the same as in the study of carb-
anion equilibrium reactions. The mixture of the alkali salt of 2-
ethylpyridine and the appropriate dimer, trimer, or tetramer was

terminated with either methyl iodide or methanol distilled in vacuo. After work-up, the crude product mixture was analyzed by capillary gas chromatography to determine product distributions. To identify the structures of the products, the crude mixture was separated by preparative liquid chromatography and each fraction analyzed by ^{1}H NMR.

Since the products in the gas chromatograph were detected by flame ionization, the integrated areas of each product peak had to be corrected to take into account the different molecular formulas. The response of the detector was dependent on the number of carbons in the molecule as well as the oxidation state of each carbon. Using "effective carbon numbers,"[26] the following values were assigned to each product:

CH_3	CH_2CH_3	CH_3CHCH_3	$CH_3CHCH_2CH_2$
(5.75)	(6.75)	(7.75)	(13.50)

$CH_3CHCH_2CHCH_3$	$CH_3CHCH_2C(CH_3)_2$	$CH_2CH_2C(CH_3)_2$
(14.50)	(15.50)	(14.50)
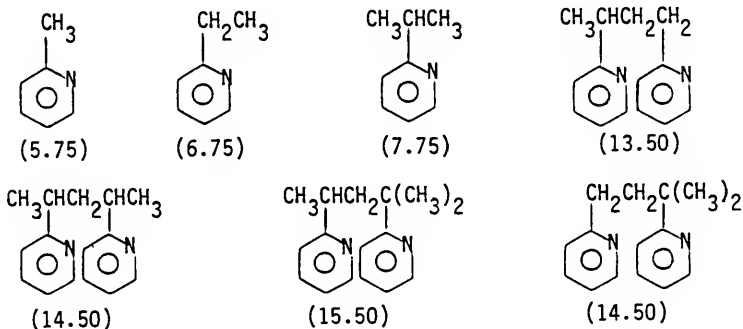
Effective Carbon Numbers[26]

C (aliphatic, aromatic)   1.0

N (tertiary amines)   -0.25

Thus, a dimer with an "effective carbon number" of 15.50 would give an integrated GC peak area twice as large as 2-isopropylpyridine, which has a value of 7.75. Taking these values into account, a reasonable determination of product distributions can be made from a GC trace.

This method was verified by using known mixtures of 2-ethylpyridine and dimer [6]. The measured and calculated GC peak areas were in good agreement (± 3%).

Preparative Liquid Chromatography

All preparative separations were performed with an Altex Model 332 programmable gradient system, fitted with a constant wavelength UV detector (254 nm). For the separation of one gram or less of a sample, a Lobar B column (E. Merck) with 40-63 μ LiChroprep Si60 silica gel was used. Generally, the eluents were programmed from non-polar (hexanes) to polar (4:1 methylene chloride:methanol) over a period of from 150 to 400 minutes,[21] depending on the sample.

Capillary Column Gas Chromatography

Gas chromatographic analyses were performed with a temperature programmable Hewlett-Packard Model 5880A instrument equipped with a flame ionization detector. The columns used were 25 or 50 meter SE-54 silicone gum (Hewlett-Packard) with a temperature limit of 350°C. Helium or hydrogen was used as the carrier gas.

Nuclear Magnetic Resonance

Proton NMR spectra (60 MHz) were obtained on either a Varian A-60A or a Varian EM-360L spectrometer. Carbon-13 (25 MHz) and 100 MHz proton NMR spectra were obtained on a Jeol JNM-FX-100 instrument. A Nicolet NT-300 NMR spectrometer (financed by the Instrument Program of the NSF Chemistry Division) was used to obtain the 300 MHz proton NMR spectra. Chemical shifts are expressed in parts per million (ppm) downfield from tetramethylsilane (TMS) unless otherwise stated. Coupling constants (J) are expressed in Hertz (Hz).

CHAPTER III

ADDITION OF ELECTROPHILES TO LIVING 2-VINYLPYRIDYL DIMER

In order to further elucidate the mechanism of the anionic oligo-
merization of 2-vinylpyridine, reactions of the 1,3-di(2-pyridyl) bu-
tane anion lithium salt [3] with various electrophiles have been
studied. The general reaction scheme is shown in Equation 1. In this
case, the living oligomers are terminated by addition of an electro-
philic species other than methyl iodide.

After isolation by preparative liquid chromatography, the dimers
[13] were analyzed by ^{1}H NMR. It was previously determined[19,21] in
the case of the symmetrical methylated dimer [6] that the meso stereo-
isomer gives a methyl doublet which is shifted downfield from the
racemic doublet. The dimers terminated with various electrophiles all
give two methyl doublets, the most intense of which is the furthest
downfield. Therefore, by comparison with the methylated dimer, it is
likely that the predominant stereoisomer in all cases is the meso-like
product.

$CH_3CHCH_2CH - R$

[13]

$R = -CH_2CH_3$, $-CH(CH_3)_2$,
$-Si(CH_3)_3$, $-CH_2Ph$,
$-CHPh_2$, $-CHPhOH$,
$-C(CD_3)_2OH$, $-CH_2CPh_2H$,
$-CH_2CH_2(2Py)$,
$-CH_2CH_2(4Py)$

30
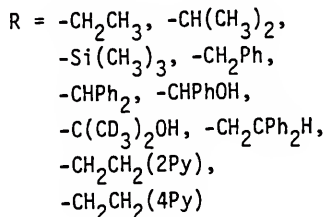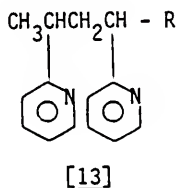
The capillary gas chromatography results indicate that the pre-
dominant stereoisomer of [13] in all cases is retained the longest on
the column. With the methylated dimer [6], it was observed[20,21] that
the stereoisomer with the longest retention time was the meso isomer.
Thus, since the predominant stereoisomer in each case follows the same
NMR and GC trends, it may be inferred that the stereochemical assign-
ments for [13] are consistent with those for [6].[20,21] That is, the
stereoisomer having the longest GC retention time and the most down-
field methyl doublet in the ^{1}H NMR has the same relative configuration
as meso-[6].

Quantitative measurements of stereochemistry were made with capil-
lary GC by using the integrated areas of the dimer peaks in the crude
oligomer mixture before isolation of the dimer. Dimer samples iso-
lated by preparative liquid chromatography were not used for quantita-
tive determinations since the stereoisomeric ratios of the isolated
dimer may be changed somewhat by LC peak shaving. However, in general
no large differences in the proportion of stereoisomers were found be-
tween the crude oligomer mixture and isolated dimer fractions.

Table 5 lists the stereochemical results determined by ^{1}H NMR
and capillary GC for the reaction of various electrophiles with the
lithio salt of [3]. It can be seen that alkyl halides generally add
in a highly stereoselective fashion. Steric bulk appears to play a
small role in the stereochemistry of alkylation, with methyl halides
reacting more stereoselectively than primary and secondary halides.
Moreover, methylation stereoselectivity appears to be independent of
the nature of the halide ion and the time allowed before termination of
the living oligomers.

Table 5

Stereochemistry of Electrophilic Addition
to 2-Vinylpyridyl Dimer Lithio Salt [3][a]

| Electrophile	Configuration (A)	(B)	Electrophile	Configuration (A)	(B)
CH_3I	>99	<1	4-Vinylpyridine	97.0	3.0
CH_3I[b]	99.1	0.9	ϕ_2CHCl	96.1	3.9
CH_3I[c]	96.6	3.4	$(CH_3)_2CHBr$	95.4	4.6
CH_3I[d]	98.2	1.8	1,1-Diphenyl-ethylene	92.7	7.3
CH_3I[e]	>99	<1	1,1-Diphenyl-ethylene[f]	63	37
CH_3Br	99.0	1.0	$(CD_3)_2CO$	84.8	15.2
CH_3Cl	99.0	1.0	ϕCHO	71.3	28.7
ϕCH_2Cl	98.0	2.0	2-Vinylpyridine	64	36
CH_3CH_2I	97.8	2.2			
$(CH_3)_3SiCl$	97.3	2.7			

[a] In THF, -78°C.
[b] 0.3 Equivalents $LiB\phi_4$ added after monomer addition.
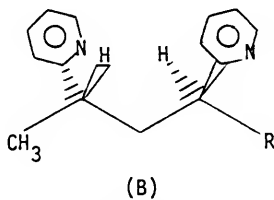[c] 1.0 Equivalent 2-ethylpyridine added after monomer addition.
[d] 1.0 Equivalent 1,3-di(2-pyridyl)butane added after monomer addition.
[e] Terminated 3 hours after completion of monomer addition at -78°C.
[f] At 25°C.

(A)

meso-like

(B)
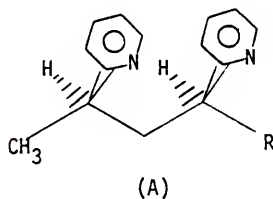
racemic-like

Addition of vinyl compounds to [3] provides some interesting re-
sults. High stereoselectivity is observed with 4-vinylpyridine and
1,1-diphenylethylene addition, while 2-vinylpyridine addition is rather
non-stereoselective. At room temperature, 1,1-diphenylethylene also
adds non-stereoselectively. It is clear from these results that fac-
tors other than steric bulk play a role in the stereoselectivity of
addition of vinyl compounds to [3]. Carbonyl compounds (benzaldehyde
and acetone-d_6) similarly add to [3] in a rather non-stereoselective
fashion.

It is interesting to note that in all cases the predominant
stereoisomer appears to have the same relative configuration as meso-
[6]. This indicates that the ion pair configuration leading to meso
placement of the electrophile or monomer is favored. Thus, cation
side attack of an electrophile on ion pair [9] (Figure 3) leads to a
meso dyad, whereas cation side attack on [10] leads to a racemic place-
ment. Intramolecular coordination of the metal ion by the nitrogen
lone pair of the penultimate pyridine ring has been evoked to explain
the predominance of ion pair diastereomer [9] over [10].[11,17-20] Non-
bonded interactions between the methyl group and the ultimate pyridine
ring as well as butane-gauche interactions in [10a] render this struc-
ture less favorable than [9a] (Figure 3).[11,19]

Figure 10 shows a scheme which appears to be consistent with the
observed differences in stereoselectivity seen in Table 5. Dimer anion
[3] presumably favors ion pair diastereomer [9] which is in equilib-
rium with a small amount of [10] (Figure 3). In addition, ^{1}H and [13]C
NMR studies have shown that anion [3] exists as a 1:1 mixture of the E
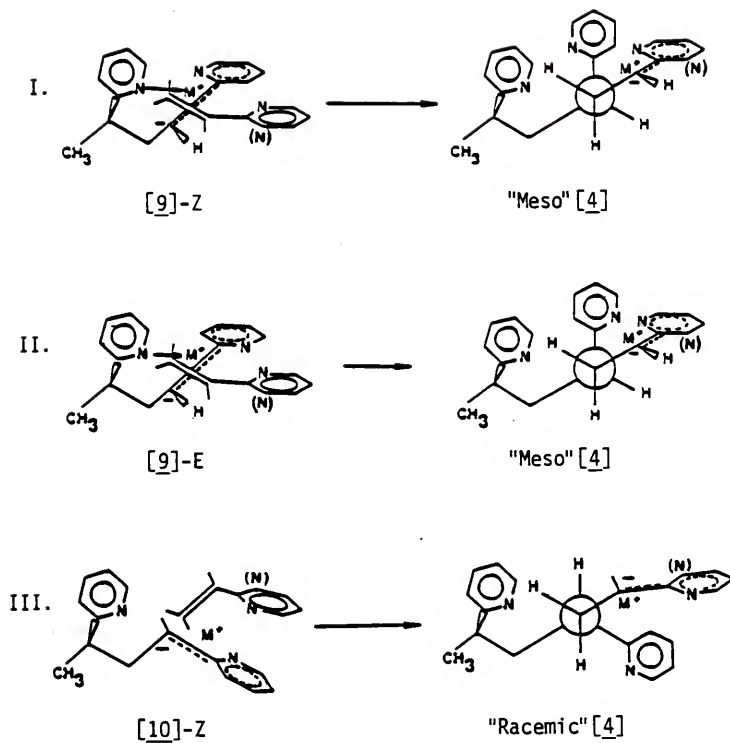
34

Figure 10. Pathways Leading to "Meso" and "Racemic" [4].

and Z isomers,[10] which equilibrate very slowly on the NMR time scale.[7,9] Thus, addition of 2-vinylpyridine to [9]-E and [9]-Z yields meso anion [4]. The transition states in these two pathways differ in that the metal ion remains intramolecularly coordinated in the addition to [9]-E (pathway II), while the penultimate pyridine nitrogen is not in proper position to coordinate the metal ion in pathway I. The two transition states are shown in Figure 11. Since intramolecular coordination is a strongly favored process, the contribution from pathway I would be expected to decrease. Therefore, since [10]-Z is in equilibrium with [9]-Z, pathway III may compete favorably with pathway I, thus increasing the overall racemic content in the product. Alternatively, reaction of 2-vinylpyridine with the uncomplexed dimer anion [3], which may be present in small amounts in this system, may overtake pathway I. Uncomplexed [3] would be expected to give a random placement of monomer, and contribution from this species may account for the lowered stereoselectivity of 2-vinyl-pyridine addition.

For electrophiles such as alkyl halides, 4-vinylpyridine, and 1,1-diphenylethylene, intramolecular coordination with the penulti-mate pyridine nitrogen in the transition state does not appear to be advantageous. As a result, these electrophiles are expected to react equally well with [9]-Z and [9]-E. The high meso addition stereo-selectivity with these electrophiles is clearly consistent with the predominance of ion pair structure [9] over [10].

In the transition state for alkylation of [3], intramolecular cation coordination will probably not be important since there is no
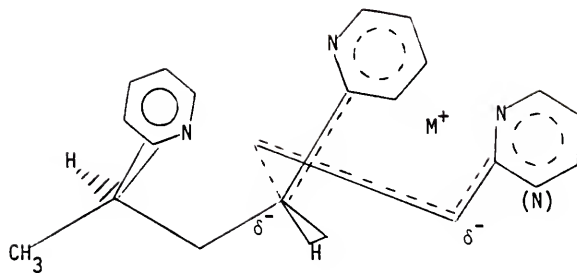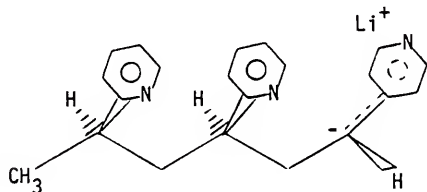
[9]-Z
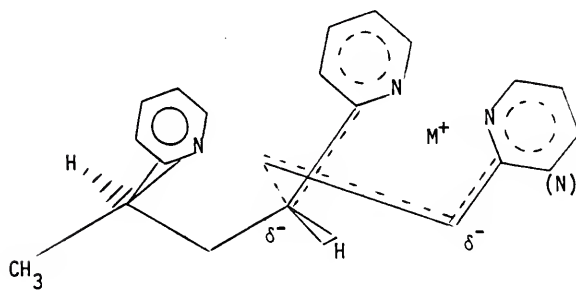
[9]-E

Figure 11. Transition States for Formation of "Meso" [4].

new carbanion formed which may benefit from the stabilization caused by such coordination. With 4-vinylpyridine addition, cation coordination will also be unimportant since the structure of the trimeric anion formed after monomer addition would probably not allow intra-

molecular coordination to occur. The newly formed 4-pyridyl carbanion would be highly delocalized, with a large charge density on nitrogen.[27] The position of the Li^+ counterion will be influenced by this delocalization and may be located too far from the penultimate pyridine ring to be coordinated. This is consistent with the non-stereoselective methylation of the 1-(4-pyridyl)-3-(2-pyridyl)butane lithio salt.[11] Here the lack of coordination of Li^+ by the penultimate 2-pyridine ring leads to a 50/50 mixture of stereoisomers. Thus, the lack of intramolecular cation coordination in the transition state for the addition of 4-vinylpyridine to [3] leads to stereoselective placement in a fashion similar to alkyl halides.

1,1-Diphenylethylene addition also supports the above scheme since it adds to [3] with high meso-selectivity at -78°C. This is the case since the diphenylmethyl anion has been shown to exist predominantly as a solvent separated ion pair at low temperatures.[28] Coordination of the Li^+ by penultimate pyridine in this case would have
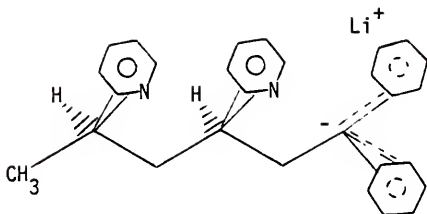
[14]

essentially no stabilizing effect on anion [14], and one would expect
that intramolecular coordination would be unimportant in the transi-
tion state as well. At 25°C, however, anion [14] would be expected to
exist predominantly as a contact ion pair,[28] and intramolecular coor-
dination in the transition state is expected to be a factor. There-
fore, addition of 1,1-diphenylethylene to [3] at 25°C results in a
relatively non-stereoselective placement similar to 2-vinylpyridine
addition.

Addition of carbonyl compounds to [3] leads to intermediate ster-
eoselectivity of placement. The Li$^+$ may be coordinated by the penul-
timate group in the transition state, but perhaps not to the same de-
gree as with 2-vinylpyridine and 1,2-diphenylethylene (at 25°C). This
is most likely due to the tightness of the O-Li bond which may de-
crease the extent of intramolecular coordination.

To verify that complexation by the penultimate pyridine is in-
deed responsible for the high meso methylation stereoselectivity, one
equivalent of 2-ethylpyridine was added to the living oligomer mixture
before termination with methyl iodide. The 2-ethylpyridine may com-
pete with the penultimate pyridine group for complexation of the Li$^+$
ion, thus disrupting intramolecular coordination. This is indeed what

is observed since the methylation stereochemistry drops significantly in the presence of one equivalent of 2-ethylpyridine (Table 5). The stereoselection is still rather high (~28/1) and is probably due to a large amount of residual intramolecularly coordinated dimer anion. It was thought that 1,3-di(2-pyridyl)butane [15] might act as a bidentate ligand and be even more effective than 2-ethylpyridine in competing with the penultimate pyridine for the Li$^+$. However, addition of one equivalent of [15] to the living oligomer system before methylation decreases stereoselection to a lesser extent than with the addition of 2-ethylpyridine (Table 5). Apparently [15] is a poorer ligand than 2-ethylpyridine, perhaps with only one of its pyridine groups coordinating to the Li$^+$. In any case, these results provide further evidence that the presence of the intramolecular coordination is responsible for the high methylation stereoselectivity of dimer anion [3].

CHAPTER IV

ANIONIC OLIGOMERIZATION OF 4-VINYLPYRIDINE

In light of the results presented in the previous chapter on the mechanism of the anionic oligomerization of 2-vinylpyridine, the stereochemistry of the corresponding oligomerization of 4-vinylpyridine (Equation 3) would be of interest. Preliminary results[17] have indicated that methylation of the dimer anion [18] is non-selective (~50/50 meso/racemic), but information on monomer addition stereochemistry or methylation of the higher oligomers has not been previously reported.

$$[16]$$

$$CH_3CHR^-, Li^+ \xrightarrow{\quad R \quad} H{-}(CH_2CHR)_n{-}CH_2CHR^-, Li^+ \qquad (3)$$

$$[17] \qquad\qquad\qquad [18] - [20]$$

$$H{-}(CH_2CHR)_n{-}CH_2CHRCH_3 \qquad H{-}(CH_2CHR)_{n+1}{-}H$$

$$[21] - [23] \qquad\qquad [24] - [26]$$
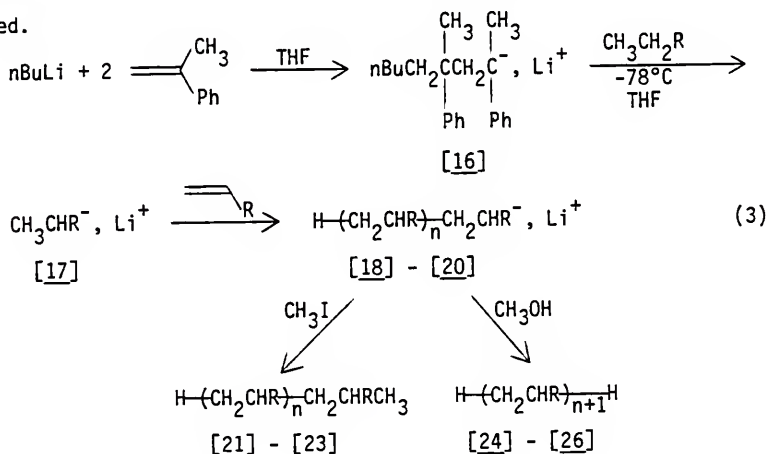
R = 4-pyridyl; [18], [21], [24] n = 1; [19], [22], [25] n = 2; [20], [23], [26] n = 3.

40

Results

Since intramolecular coordination of the Li^+ ion by the penulti-
mate pyridine nitrogen would not be plausible in the 4-vinylpyridyl
oligomerization, the stereoselectivity of methylation and 4-vinylpyri-
dine addition would be expected to decrease with respect to that in
the 2-vinylpyridyl oligomerization.[19] To probe this, the reactions in
Equation 3 were carried out. The living 4-vinylpyridyl oligomers were
terminated with methanol to determine the stereochemistry of vinyl ad-
dition, whereas the methylated products were used to determine both
the monomer addition and methylation stereochemistry. Stereochemical
assignments were made by isolation of the individual oligomers by
preparative liquid chromatography and analysis of their ^1H and ^{13}C NMR
spectra. Analyses of the proportions of the various stereoisomers
were made by integration of the capillary GC peak areas in the crude
oligomer product mixtures.

Figure 12 shows the 100 MHz ^1H NMR spectra of the meso (m) and
racemic (r) isomers of [21] which were isolated by preparative liquid
chromatography. Spectrum 12a was identified as that of the meso iso-
mer due to the $AA'B_2$ methylene pattern (1.84 ppm), indicating the
magnetic non-equivalence of H_A and H_A'. The spectrum of the racemic
isomer gives an A_2B_2 pattern characteristic of equivalent methylene

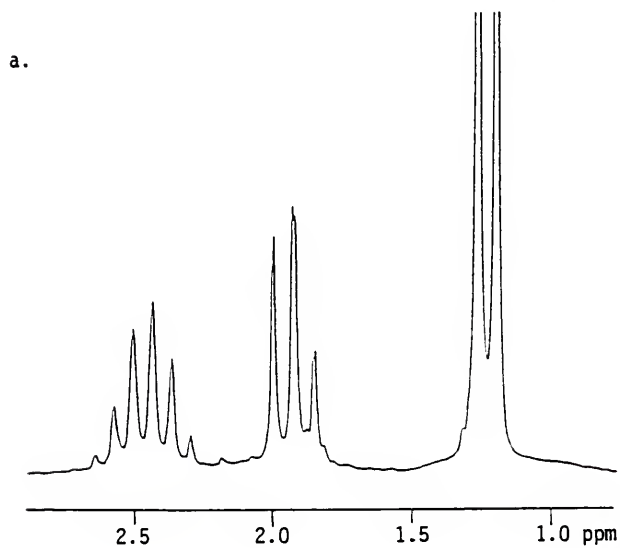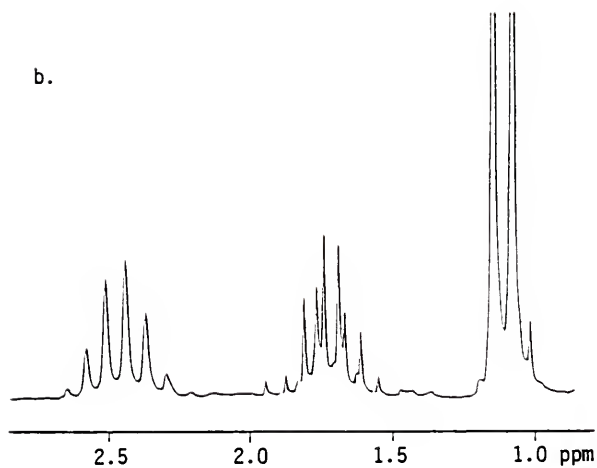meso (m)   racemic (r)
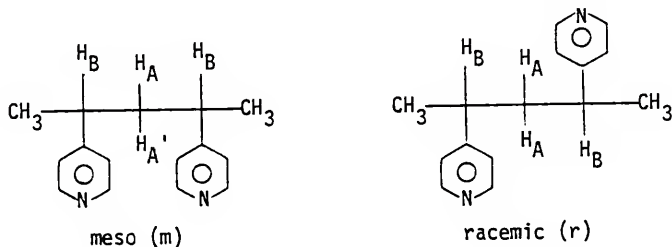
Figure 12. 100 MHz ^{1}H NMR Spectra of the (m) and (r) Stereoisomers of Dimer [21].

protons. The methyl groups in these isomers are also found to be sensitive to stereochemistry. The resonances of the meso isomer (1.25 ppm) are shifted somewhat downfield from the racemic isomer (1.17 ppm). These NMR spectra are very similar to those previously reported for the (m) and (r) stereoisomers of 2,4-diphenylpentane [27][29,30] and 2,4-di(2-pyridyl)-pentane [6][19,31] (Table 6).

CH₃CHCH₂CHCH₃ (placeholder)
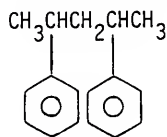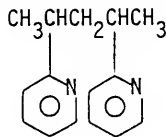
[27]   [6]

In the ^{13}C NMR spectra of the meso and racemic isomers of [21], several resonances are found to be sensitive to stereochemistry (Table 7). The methyl carbon is particularly sensitive to stereochemistry, with the (m) resonance shifted upfield from that of the (r) isomer. This trend is also seen in [6],[20,21] [27],[32-35] and 2,4-bis(4-bromophenyl)pentane.[36] The (m) and (r) stereoisomers of [21] are also detectable by capillary gas chromatography, with the (r) isomer eluting first. From the GC of the dimer in the crude oligomer mixture (before isolation by LC), the stereochemistry of methyl addition was found to be rather non-selective (60% meso/40% racemic).

In assigning the stereochemistry of the trimer [22], three stereoisomers are possible: isotactic (mm), heterotactic (mr), and syndiotactic (rr). Four methyl resonances are expected in the NMR of this trimer, one for each of the symmetrical isomers (mm) and (rr) and

Table 6

Chemical Shifts and Approximate Splittings for 2,4-Disubstituted Pentanes

	Solvent	T (°C)	CH_3	H_A	H_A'	Approximate Splittings (Hz)				Reference
						CH_3-CH	AB	A'B	AA'	
meso-[27]	CCl_4	35	1.21	1.71	1.92	6.8	7.5	7.5	13.6	29
meso-[21]	$CDCl_3$	25	1.25	1.75	1.94	6.8	7.9	7.2	13.7	this work
meso-[6]	CCl_4	25	1.24	1.77	2.25	6.8	7.3	6.9	13.3	19
racemic-[27]	CCl_4	35	1.15	1.88	1.88	6.8	10.0	5.0	-	29
racemic-[21]	$CDCl_3$	25	1.17	1.89	1.89	6.7	7.8	7.5	-	this work
racemic-[6]	CCl_4	25	1.17	2.08	2.08	6.7	7.8	7.0	-	31

Table 7

^{13}C NMR Chemical Shift Assignments for (m) and (r) [21]

Carbon	shift (ppm)	
	(m)	(r)
CH_3	21.42	22.57
CH_2	45.30	44.94
CH	36.97	37.31
C_4	155.81	155.55
C_3, C_5	122.33	122.60
C_2, C_6	150.01	150.04

two for the unsymmetrical isomer (mr). In the ^{1}H spectrum, the four methyl doublets complicate the assignment of stereoisomers (Figure 13). However, in the ^{13}C spectrum all four methyl absorptions are easily distinguished (Figure 14). By comparison with the dimer, the two upfield peaks should be due to stereoisomers with an (m) dyad adjoining the CH_3 group (mm and rm) and the two downfield peaks due to the isomers with an (r) dyad adjoining the CH_3 group (rr and mr). The stereochemical assignments, in accord with the ^{13}C NMR results for 2,4,6-triphenyl-heptane,[32-34] 2,4,6-tri(2-pyridyl)heptane,[20,21] and 2,4,6-tris(4-bromophenyl)heptane,[36] are then as follows: (mm) 20.3 ppm, (rm) 20.6 ppm, (rr) 22.5 ppm, and (mr) 22.9 ppm (Table 8).

Figure 13b shows the 100 MHz ^{1}H NMR spectrum of the isotactic stereoisomer of trimer [22] isolated by collecting only the last por- tion of the trimer fraction in the preparative LC separation of 4- vinylpyridyl oligomers. The methylene region of this spectrum shows
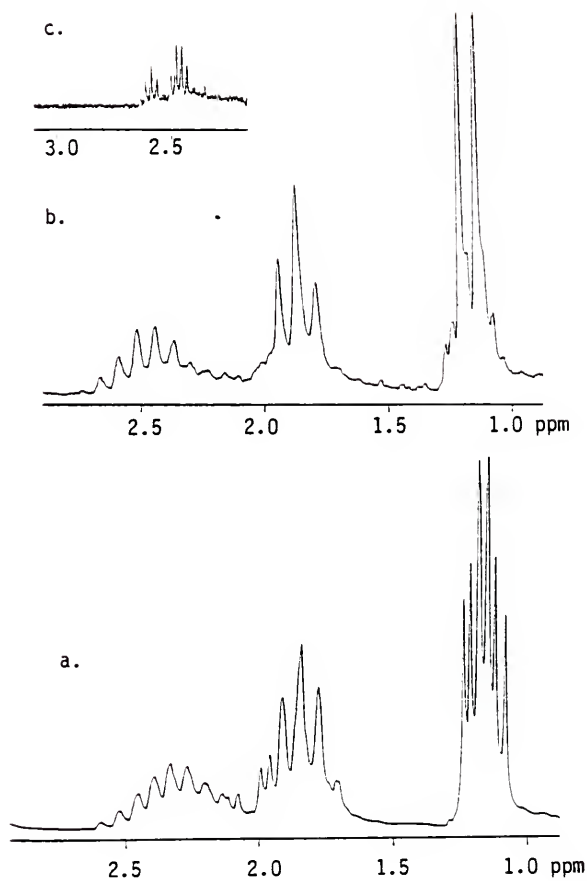
46

Figure 13.   100 MHz ^{1}H NMR Spectra of Trimer [22]; a) mixture of
all three stereoisomers, b) isotactic [22], c) 300
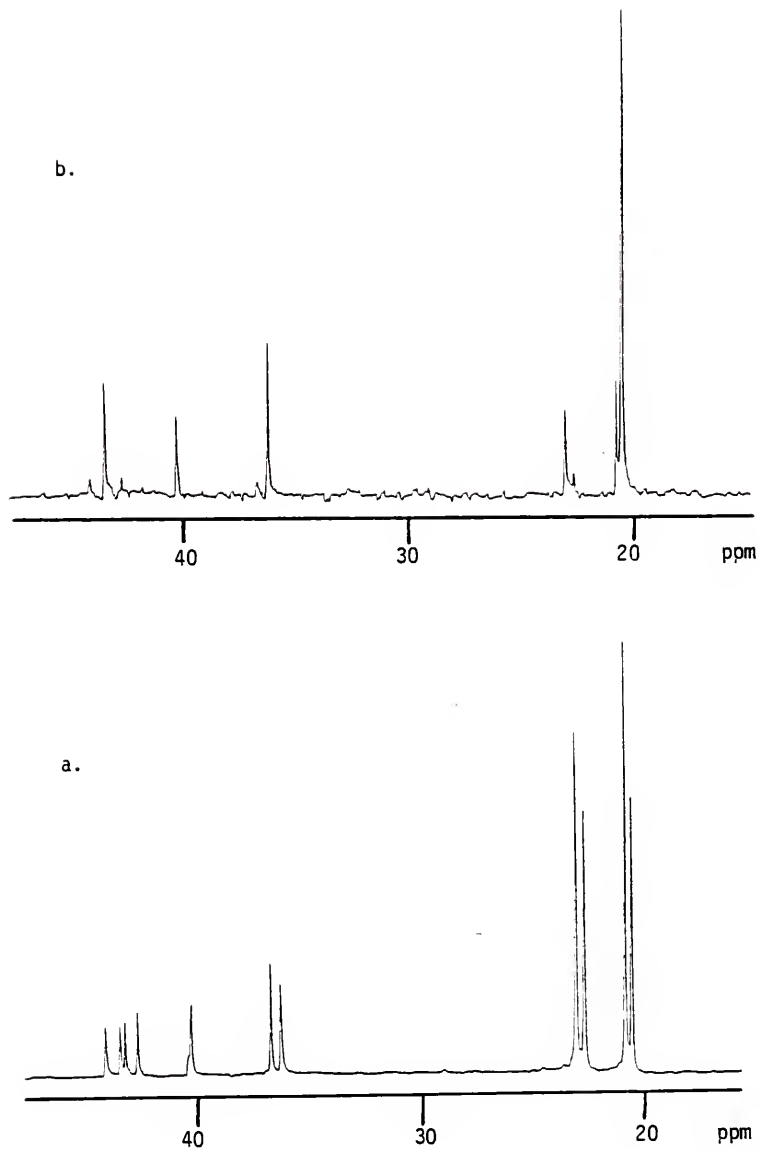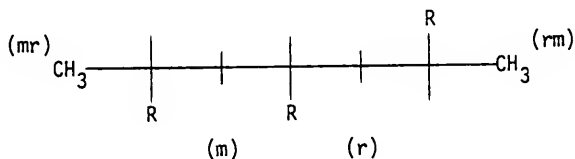MHz ^{1}H spectrum of isotactic [22].

47

Figure 14.   25.2 MHz ^{13}C NMR Spectra of Trimer [22]; a) mixture of
all three stereoisomers, b) predominantly isotactic [22].

Table 8

^{13}C Chemical Shifts for the Methyl Carbons in [22], [7],
2,4,6-Triphenylheptane (2,4,6-TPH)
and 2,4,6-Tris(4-bromophenyl)heptane (2,4,6-TBPH)

	(mm)	(rm)	(mr)	(rr)	References
[22]	20.3	20.6	22.9	22.5	this work
[7]	20.5	20.8	22.4	21.9	20,21
2,4,6-TPH	21.2	21.3	23.8	23.4	32,33
2,4,6-TBPH	21.1	21.7	23.7	23.3	36

a simple triplet pattern which indicates that the geminal CH_2 protons
as well as the CH_2-CH coupling constants are nearly equivalent. The
situation is very similar in the spectrum of isotactic 2,4,6-tri-
phenylheptane.[37,38] In contrast to this, H_A and H_A' are non-equiva-
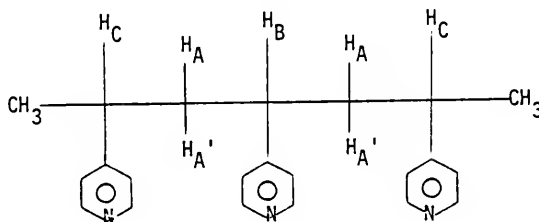
[22]

lent in the spectrum of isotactic 2,4,6-tri(2-pyridyl)-heptane [7].[19]
Moreover, the CH_2-CH coupling constants, J_{AC} and J_{AB}, are unequal in

[7], resulting in a complex CH_2 spectrum. The position of the pyridine nitrogen atoms in [7] and [22] appears to have different effects

[7]

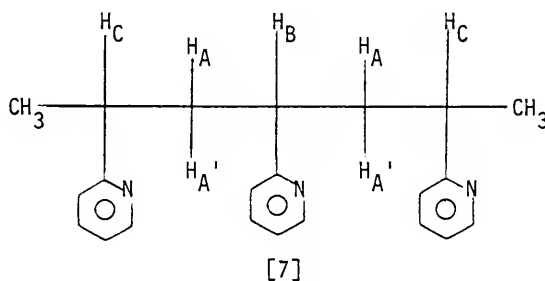on the NMR spectra of the backbone protons. Thus, the various stereoisomers of [22] would be expected to give spectra similar to those for 2,4,6-triphenylheptane. On this basis, the spectrum in Figure 13b is shown to be consistent with the isotactic stereoisomer of [22] as assigned by ^{13}C NMR.

Table 9

CH$_2$ Chemical Shifts and Approximate Splittings for
Isotactic Trimers [7], [22] and 2,4,6-Triphenylheptane (2,4,6-TPH)

Trimer	(ppm) A	A'	Approximate Splittings (Hz) AC	AB
[7][a] 19	1.90	2.17	7.9	5.7
[22][b]	1.88	1.84	7.2	7.4
2,4,6-TPH[c] 38	1.69	1.65	8.2[d]	5.9[d]

[a] In CCl_4, 25°C.

[b] In $CDCl_3$, 25°C.

[c] In o-dichlorobenzene, 70°C.

[d] The splittings are approximately equal in CCl_4 at 25°C.[37]

The 300 MHz ^{1}H NMR spectrum of the CH protons of isotactic [22] is shown in Figure 13c. These protons give a hextet and pentet in a ratio of 2:1, corresponding to H_C and H_B, respectively. The observed pattern is consistent with the symmetrical nature of the isotactic trimer. In the methyl region of the ^{13}C NMR spectrum of predominantly isotactic [22] (Figure 14b), the isotactic (mm) resonance is observed to be the furthest upfield, with small peaks for the (mr), (rm) and (rr) isomers which are present in small quantities.

The GC results (Figure 15) indicate that the three trimer stereoisomers in the product exist in a 1:2:1 ratio, with the isotactic isomer corresponding to the last eluted peak. Furthermore, GC analysis of the protonated 4-vinylpyridyl oligomers (Equation 3, [24] - [26]) indicates the presence of two trimer stereoisomers in a ratio of 1.15/ 1.0 (54% meso/46% racemic). Hence, a totally random stereochemistry of addition of both the monomer and methyl iodide is indicated. The assignment of trimer peaks in the GC should then be (in order of elution): (rr), (mr, rm) and (mm). This random stereochemistry is not unexpected since methylation of 4-vinylpyridyl dimer anion [18] is found to be non-stereoselective (60/40).

Since the stereochemistry of methylation and monomer addition in trimer is essentially random, one would expect to see equal amounts of each possible stereoisomer in the NMR spectrum of tetramer [23]. Figure 16 shows the ^{13}C NMR spectrum of [23] isolated by preparative LC. Six methyl absorptions are observed indicating that not all of the eight possible methyl absorptions (mmm, mmr, mrm, rmm, mrr, rmr, rrm and rrr) are resolved. Following the trend for dimer and trimer, the
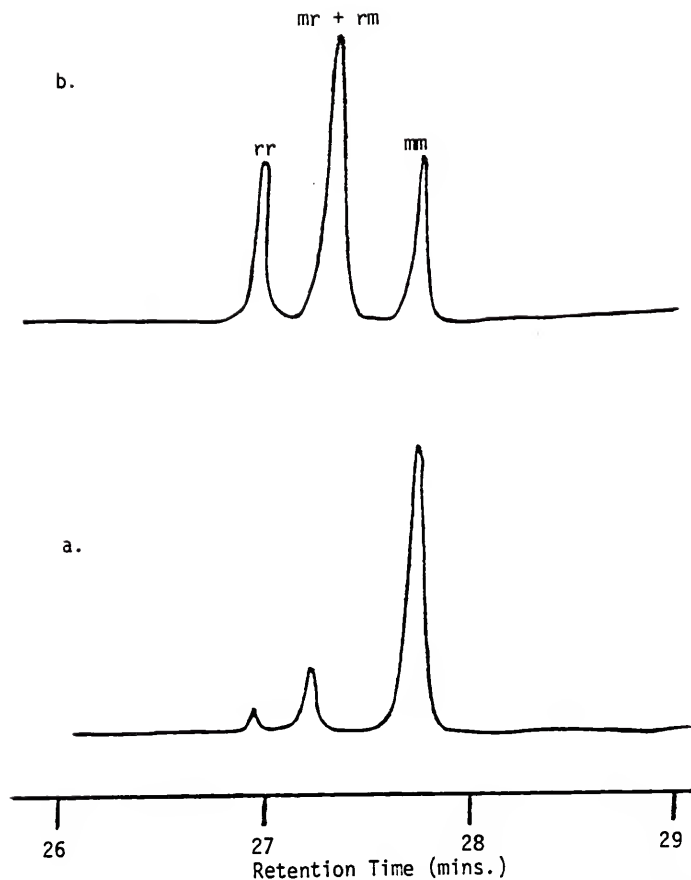
51

Figure 15. Capillary GC Traces for Trimer [22]; a) predominantly
isotactic [22] (from NMR spectrum in Figure 13), b)
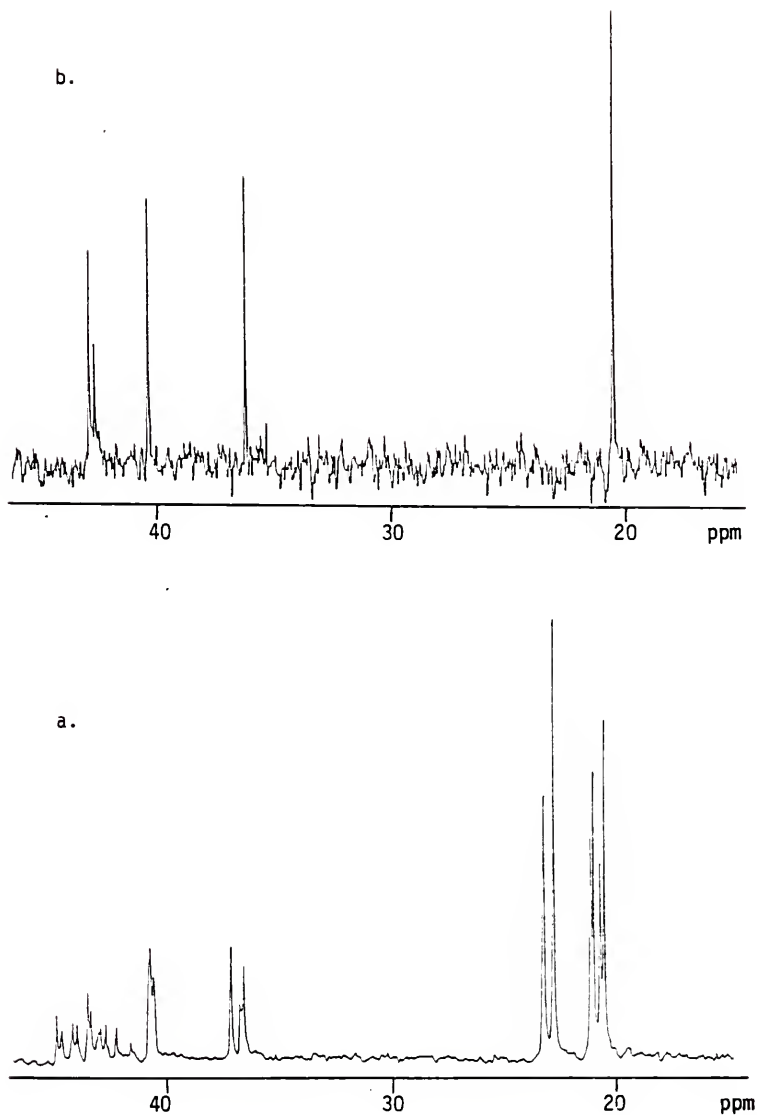trimer stereoisomers in oligomerization product.

Figure 16.   25.2 MHz ^{13}C NMR Spectra of Tetramer [23]; a) mixture of all stereoisomers, b) isotactic [23].

group of 4 upfield absorptions (20-21 ppm) correspond to the CH_3 groups adjoining an (m) dyad, and the two downfield peaks (22.5-23.0 ppm) correspond to those adjoining an (r) dyad. The peaks may be assigned further by analogy with the trimer assignments (Figure 14). That is, methyl groups adjoining (mm), (rm), (rr), and (rm) triads absorb from high field to low field, respectively. The upfield set of peaks are further resolved into tetrads and are tentatively assigned as (mmm), (rmm), (rrm), and (mrm) from high to low field on the basis of a comparison with the corresponding 2-pyridyl tetramer.[20,21] Table 10 lists the ^{13}C NMR methyl chemical shifts and their stereochemical assignments for tetramer, [23], and the corresponding 2-pyridyl and phenyl analogues.

Table 10

^{13}C Methyl Chemical Shifts for Tetramers
[23], [8], and 2,4,6,8-Tetraphenyloctane (2,4,6,8-TPO)

Stereoisomer	Chemical Shifts		
	[23]	[8][21,31]	2,4,6,8-TPO[33]
mmm	20.3	20.2	20.9
rmm	20.5	20.4	21.1
rrm	20.8	20.8	21.1
mrm	20.9	20.9	21.5
(rrr, mrr)	22.6	21.6	23.2 (23.1)
(mmr, rmr)	23.0	22.3 (22.2)	23.8

To verify these assignments, a single tetramer stereoisomer was isolated by preparative LC. Figure 16b shows the ^{13}C NMR spectrum of

this tetramer stereoisomer. The methyl resonance corresponds to the most upfield peak in the methyl spectrum of tetramer [23] (Figure 16a). Thus, it is reasonable that the spectrum is that of the iso- tactic tetramer. The 300 MHz ^{1}H NMR spectrum of this stereoisomer is shown in Figure 17. The methine protons give two multiplets of
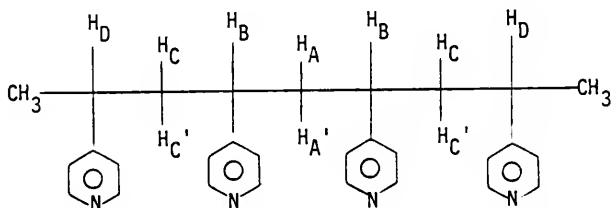
[23]

equal intensity at 2.38 and 2.48 ppm, for H_D and H_C, respectively. This simple spectrum is clearly due to the symmetrical nature of this stereoisomer. The methylene spectrum shows two multiplets in a 2:1 ratio at 1.82 and 1.95 ppm, which are assigned to $H_C(H_C')$ and $H_A(H_A')$, respectively. The geminal methylene protons are magnetically equiva- lent, as with the isotactic trimer, but the $H_C(H_C')$ protons give a more complicated spectrum than the $H_A(H_A')$ protons due to the exist- ence of two different CH_2-CH coupling constants (J_{BC} and J_{CD}). Capil- lary GC data are consistent with the assignment of this stereoisomer as isotactic, since it corresponds to the last peak eluted in the crude tetramer fraction (Figure 18).

To assign the other peaks in the GC trace to the various tetramer stereoisomers, the isotactic species was epimerized with potassium
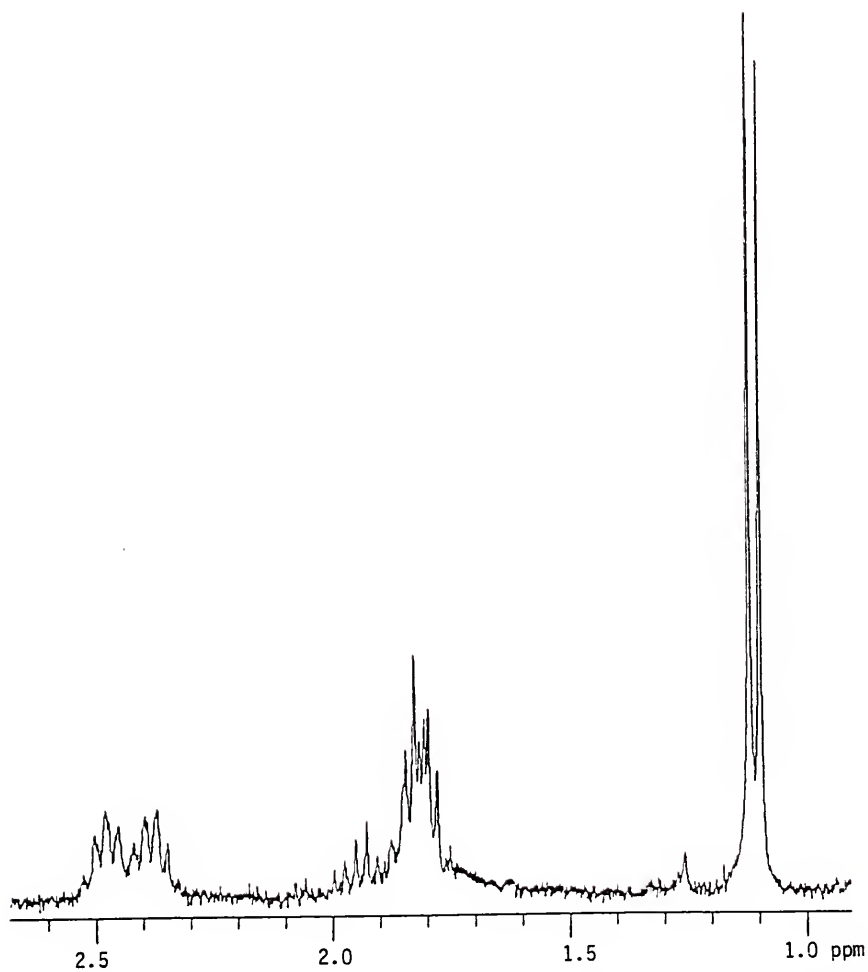
55

Figure 17. 300 MHz ^{1}H Spectrum of a Single Stereoisomer of Tetramer
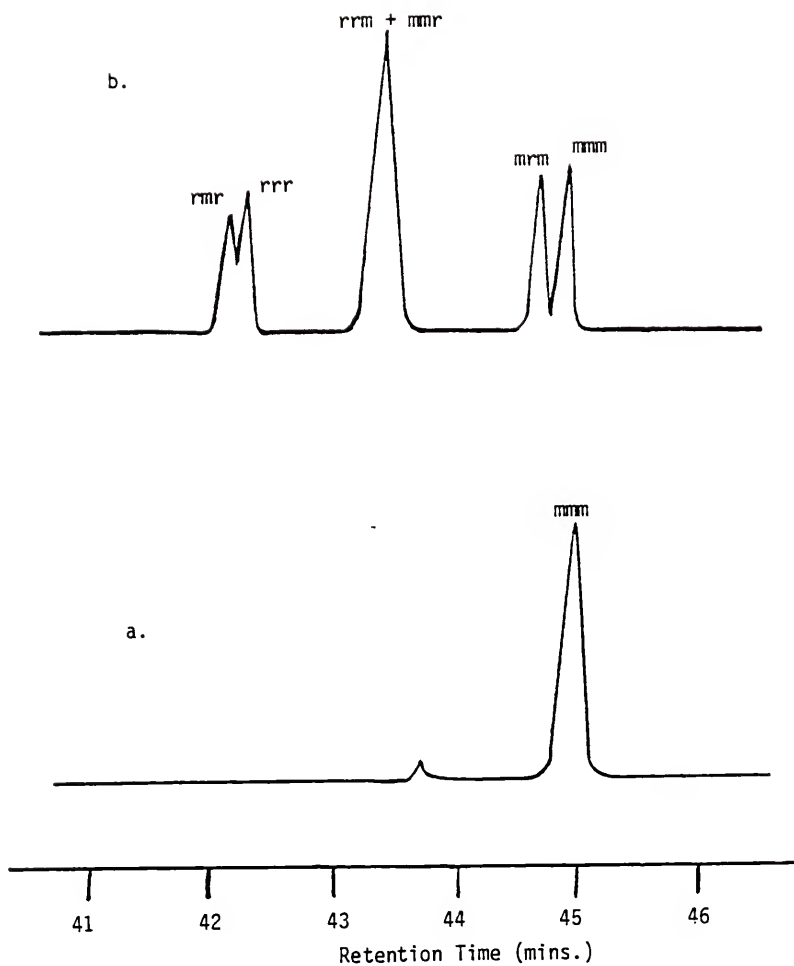[23].

Figure 18. Capillary GC Traces for Tetramer [23]; a) isotactic [23], b) tetramer stereoisomers in oligomerization product.

tert-butoxide in tert-butanol. The GC traces of the isotactic tetra-
mer epimerized for various amounts of time are shown in Figure 19.
The external asymmetric centers of [23] are expected to epimerize much
faster than the internal asymmetric centers, as observed in the epi-
merization of isotactic 2-vinylpyridine tetramer[20,21] (Scheme 1).
Therefore, the first stereoisomers formed would be (mmr) and (rmr)
with the (mrr), (mrm), and (rrr) isomers formed much more slowly. The
epimerization results show the formation of only two stereoisomers
from the isotactic tetramer which must correspond to (mmr) and (rmr),
the former being the first to appear. Apparently, epimerization of
the internal asymmetric centers is extremely slow under these condi-
tions (t-BuOK, t-BuOH, 25°C), since little epimerization appears to
take place at these positions after 2 weeks. However, the (mmm),
(mmr), and (rmr) assignments follow the same pattern as in the 2-
vinylpyridyl tetramer,[20,21] and it seems likely that the other stereo-
isomers follow as well. Thus, the order of elution for tetramer [23]
should be (rrr), (rmr), (rrm and mrr), (mmr and rmm), (mrm), (mmm)
(Figure 18).

Discussion

Table 11 summarizes the observed stereochemistry of the oligomer-
ization of 4-vinylpyridine according to Equation 3 and determined by
capillary GC. From these results, it can be seen that both methyla-
tion and monomer addition are stereochemically random. Since intra-
molecular coordination of Li^+ in the manner invoked for 2-vinylpyri-
dine oligomerization is not possible, ion pair diastereomer [28] will
not be preferred with respect to [29], and approximately equal amounts
of the two diastereomers should be present. Thus, cation side attack
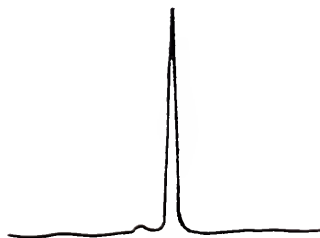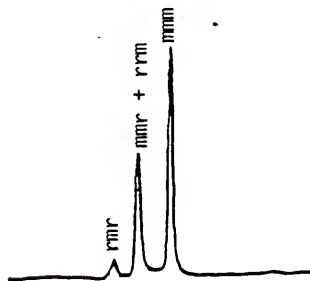
58

Isotactic

t = 0

t = 30 min.
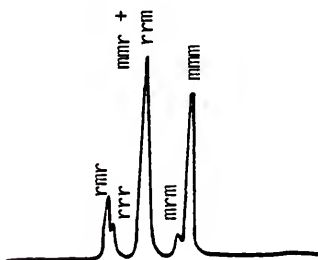
t = 8 hr.
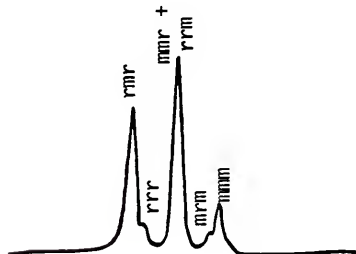
t = 210 hr.

Figure 19. Epimerization of Isotactic Tetramer [23].

Scheme 1
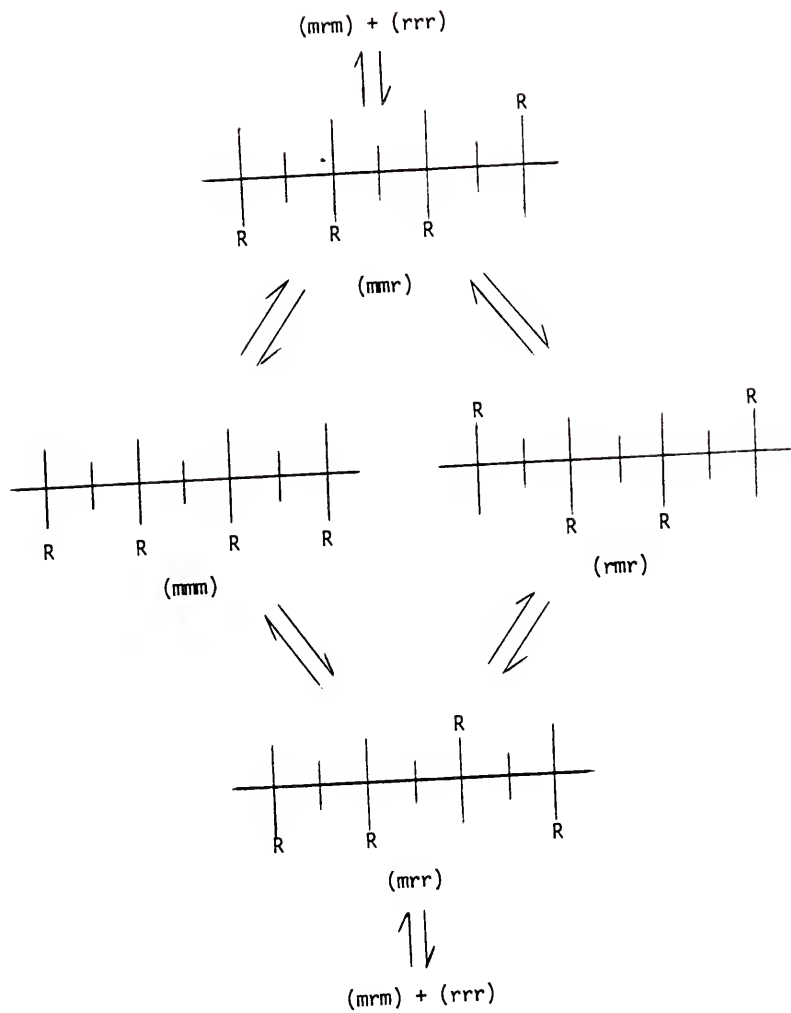
Table 11

Stereochemistry of the Anionic Oligomerization
of 4-Vinylpyridine[a] Determined by Capillary GC

Structure		%
CH_3—│—│—│—CH_3 (R, R)	(m)	59.6%
	(r)	40.4%
CH_3—│—│—│—│—CH_3 (R, R, R)	(mm)	26.9%
	(mr + rm)	51.5%
	(rr)	21.6%
CH_3—│—│—│—│—H (R, R, R)	(m)	54.0%
	(r)	46.0%
CH_3—│—│—│—│—│—CH_3 (R, R, R, R)	(mmm)	13.6%
	(mrm)	13.8%
	(mmr, rmm, rrm, mrr)	51.4%
	(rmr)	12.3%
	(rrr)	8.6%
CH_3—│—│—│—│—│—H (R, R, R, R)	(mm)	26.9%
	(rm + rr)	46.9%
	(mr)	26.2%

Reaction		Products
$CH_3CHRCH_2CHR^-$, Li^+	$\xrightarrow{CH_3I}$	60% (m), 40% (r)
"	$\xrightarrow{4VP}$	54% (m), 46% (r)
$CH_3(CHRCH_2)_2CHR^-$, Li^+	$\xrightarrow{CH_3I}$	51% (m), 49% (r)
"	$\xrightarrow{4VP}$	51% (m), 49% (r)
$CH_3(CHRCH_2)_3CHR^-$, Li^+	$\xrightarrow{CH_3I}$	51% (m), 49% (r)

[a] Li^+ counterion, -78°C, in THF.
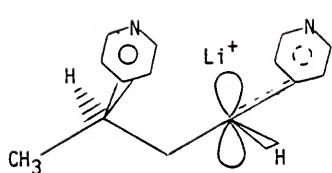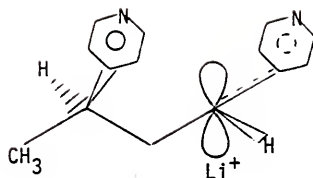
[28]   [29]

of monomer or methyl iodide will result in random stereochemistry of
placement. In accord with this, the corresponding anionic polymeri-
zation of 4-vinylpyridine leads to atactic polymer.[2,39]

Isolation and NMR analysis of the various stereoisomers of oligo-
4-vinylpyridines would serve as a great aid in assigning the observed
stereoisomeric shifts in the polymer NMR spectra. However, using
routine preparative LC techniques, only dimer stereoisomers were com-
pletely separable. Isotactic trimer and tetramer were also isolated,
although subsequent attempts to isolate these stereoisomers proved
less than satisfactory. Isolation of syndiotactic and heterotactic
trimer was difficult, and the assignment of isotactic trimer was made
largely by comparison to the NMR spectrum of isotactic 2,4,6-tri-
phenylheptane. Due to the larger number of stereoisomers, tetramer
separation proved to be an even more difficult task.

Recycle gel permeation chromatography appears promising as a
technique for isolating individual stereoisomers of 4-vinylpyridine
oligomers. Successful separations have been performed on styrene
oligomers up to pentamer.[40-42] These separations have been inter-
preted as being dependent on the differences in the predominant con-
formations adopted by these stereoisomers.[40]

It is interesting to note that the order of elution observed in the separation of styrene oligomers into diastereomers[33,35,37,40,41,43] follows the same trend as for 2-vinylpyridyl oligomers[20,21] using either LC or GC. The general order of elution is listed in Table 12.

Table 12

Order of Elution of Stereoisomers
of Styrene and 2-Vinylpyridine Oligomers

	Dimer	Trimer	Tetramer
first eluting		(rr)	(rrr)
	(r)		(rmr)
		(rm)	(rrm)
			(rmm)
	(m)	(mm)	(mrm)
last eluting			(mmm)

The same elution order is followed in the GC and LC of 4-vinylpyridine dimer, while the isotactic trimer and tetramer are the last stereoisomers to elute in the trimer and tetramer fractions, respectively. Thus, the remaining stereoisomers may be assigned with the same degree of confidence by comparison of the chromatographic data to the 2-pyridyl and phenyl analogues.

In addition to the chromatographic similarities, the ^{1}H and ^{13}C NMR shifts of the various stereoisomers of 4-vinylpyridine oligomers appear to follow the same pattern as the styrene oligomers (Tables 6-9). Thus, the NMR spectral data coupled with the chromatographic results allow a satisfactory assignment of the various 4-vinylpyridine oligomer stereoisomers.

CHAPTER V

THERMODYNAMICS OF INTRAMOLECULAR COORDINATION

In order to probe the thermodynamics of the intramolecular coordination in the anionic oligomerization of 2-vinylpyridine, the proton transfer reactions between model compounds [15], [30], [31], [6] and alkali metal salts of 2-ethylpyridyl carbanion [2] were studied (Equations 4 and 5). These proton transfer reactions result in the formation of model anions [3], [32], [33], [34] and 2-ethylpyridine.

$$CH_3CHR^-, M^+ \;+\; CH_3CHR'CH_2CH_2R \;\xrightleftharpoons[THF]{K_1}\;$$

$$[2] \qquad\qquad [15], [30], [31]$$

(4)

$$CH_3CH_2R \;+\; CH_3CHR'CH_2CHR^-, M^+$$

$$[3], [32], [33]$$

$\Big\Updownarrow K_2$

[15], [3] R = R' = 2-pyridyl

[30], [32] R = 2-pyridyl
R' = 3-methyl-2-pyridyl

[31], [33] R = 2-pyridyl
R' = phenyl

M = Li$^+$, Na$^+$, K$^+$

$$CH_3-CH \underset{R'}{\overset{CH_2}{\diagup\;\diagdown}} CHR^- \longrightarrow M^+$$

$$[3'], [32'], [33']$$

$$CH_3CHR^-, Li^+ + CH_3CHRCH_2CHRCH_3 \xrightleftharpoons{K_{app}}$$

$$[\underline{2}] \qquad\qquad [\underline{6}]$$

$$CH_3CH_2R + CH_3CHRCH_2\overset{\overset{\displaystyle CH_3}{|}}{C}R^-, M^+$$

(5)

$$[\underline{34}]$$

R = 2-pyridyl
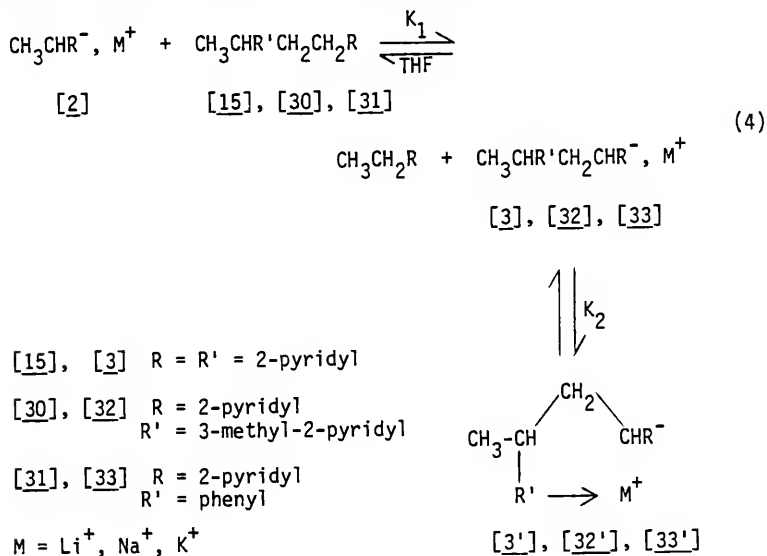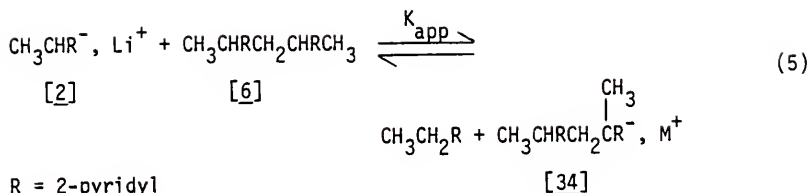
The attainment of the equilibrium was verified by measuring the change in product distribution with time. This was accomplished by rapidly alkylating each sample with ethyl iodide and determining the product distribution with capillary gas chromatography. Alkylations were carried out by in vacuo addition of CH_3CH_2I from a sealed ampule onto the stirred carbanion solution. Alkylations were complete in 1-2 seconds as determined by the rapid disappearance of the red color of the carbanion. Since the alkylations are very fast compared to the rates of proton transfer, analysis of the products should reflect the position of the proton transfer equilibrium. The apparent equilibrium constant (K_{app}) is given by

$$K_{app} = \frac{[CH_3CH_2R][CH_3CHR'CH_2CHRC_2H_5]}{[CH_3CHRC_2H_5][CH_3CHR'CH_2CH_2R]}$$

and may be expressed as $K_{app} = K_1 (1+K_2)$, where K_1 is the equilibrium constant in the absence of intramolecular cation coordination, and K_2 refers to the equilibrium between dimeric anions [$\underline{3}$], [$\underline{32}$], [$\underline{33}$], [$\underline{34}$] and their coordinated conformers [$\underline{3'}$], [$\underline{32'}$], [$\underline{33'}$] and [$\underline{34'}$]. If it is assumed that the stabilities of the carbanions are not greatly

affected by substituents beta to carbanion, it follows that $K_1 \cong 1$ so that $K_{app} \cong 1+K_2$.

Figure 20 shows the changes in the product distribution with time at 25°C with [15] as the substrate and lithio-, sodio- and potassio salts of 2-ethylpyridine (Equation 4). Again, it is clear that the approach to the proton transfer equilibrium is much slower (1-4 hours) than the alkylation (1-2 seconds). Table 13 shows that the proton transfer in Equilibrium 5 is much slower than in Equilibrium 4, apparently due to the lower kinetic acidity of the tertiary proton.

Table 13

Time Required for Establishment of
Proton Transfer Equilibria 4 and 5

Substrate	Counterion	Time
[15]	Li^+	1 hour
[15]	Na^+	4 hours
[15]	K^+	$1\frac{1}{2}$ hours
[6]	Li^+	250 hours

Table 14 lists the values of K_2 for anion [3] as a function of temperature and concentration with Li, Na, and K counterions in THF. These results indicate large values of K_2 for the lithio salts of [3], somewhat smaller values for the lithio salt of [34], and considerably
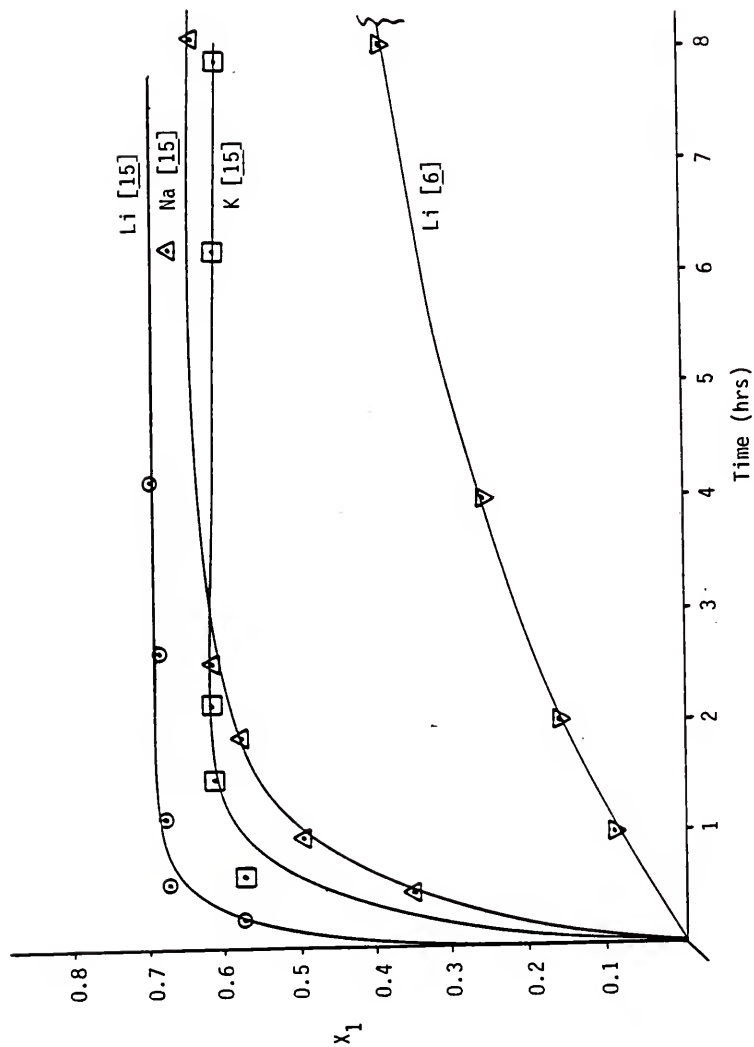
66

Figure 20. Appearance of Dimer Anion vs. Time in Proton Transfer Equilibria 4 and 5;
$X_1 = $ [Dimer Anion Concentration]/[Total Dimer Concentration].

---

intramolecular coordination. For the sodio salt, cryptation leads to a modest reduction in K_2, but interestingly addition of 18-crown-6 does not appreciably affect the equilibrium.

A decrease in K_2 is noted for the lithium salt of [34] with respect to [3], reflecting the free energy difference between tertiary and secondary α-pyridyl carbanions. From pKa values reported for protons α to phenyl,[44] carbonyl[45] or sulfone[46] groups, the tertiary carbanions are generally found to be 1-3 kcal/mol less stable than the corresponding secondary carbanions. Comparison of the K_{app} values for the formation of the lithium salts of [3] and [34] indicate that the tertiary carbanion in this case is about 0.6 kcal/mol less stable than the secondary carbanion. However, the difference in activation free energy for the formation of the lithium salts of [3] and [34] is estimated to be about 3 kcal/mol. Thus, steric factors appear to play a role in decreasing the kinetic acidity of the tertiary site. This is in agreement with earlier results on the epimerization of 2-vinyl-pyridyl oligomers.[20,21] The much slower rate of tertiary proton abstraction clearly indicates that, at least for short reaction times, very little tertiary proton abstraction occurs in the deprotonation of [15] (Equation 4).

Of particular interest is the observation that K_{app} (= 1+K_2) exceeds unity in systems where intramolecular cation coordination is expected to be absent. Thus for the lithio salts of [32] and [33], the values of K_{app} at 25°C are about 2 and 1.8, respectively, and the corresponding value for the [2.1.1] complexed lithio salt of [3] is 2.2. In the case of anion [33], intramolecular coordination of the

metal ion is clearly impossible, and this should also be the case for [3] where cryptation would prevent intramolecular coordination. For [32], such coordination has also been shown to be implausible on the basis of observed alkylation stereochemistry and by inspection of CPK molecular models.[23] Apparently, in these cases the ion pairs are stabilized by effects of a different origin, the nature of which is not yet completely clear.

Figure 21 shows a plot of ln K_2 vs. 1/T for dimer anion [3] in Equation 4, with Li^+, Na^+ and K^+ counterions. The values of ΔH and ΔS for these systems were determined from these plots and are listed in Table 15. For all counterions, ΔH is negative, becoming less negative with increasing cation size. Interestingly, ΔS has a small negative value for Na^+ and K^+ and a small positive value for Li^+. This is consistent with the displacement of coordinated solvent molecule from the cation upon coordination by the penultimate pyridine group. The entropy lost upon forming the conformationally restricted intramolecular complex would be compensated for by the entropy gained upon displacement of one or more solvent molecules from the metal ion solvation shell.

Table 15

Thermodynamic Parameters for Equation 4
Determined from a Plot of lnK_2 vs. 1/T

Counterion	ΔH (kcal/mol)	ΔS (e.u.)
Li	-1.39 ± 0.10	0.81 ± 0.40
Na	-1.29 ± 0.15	-2.60 ± 1.00
K	-0.47 ± 0.20	-0.40 ± 1.20
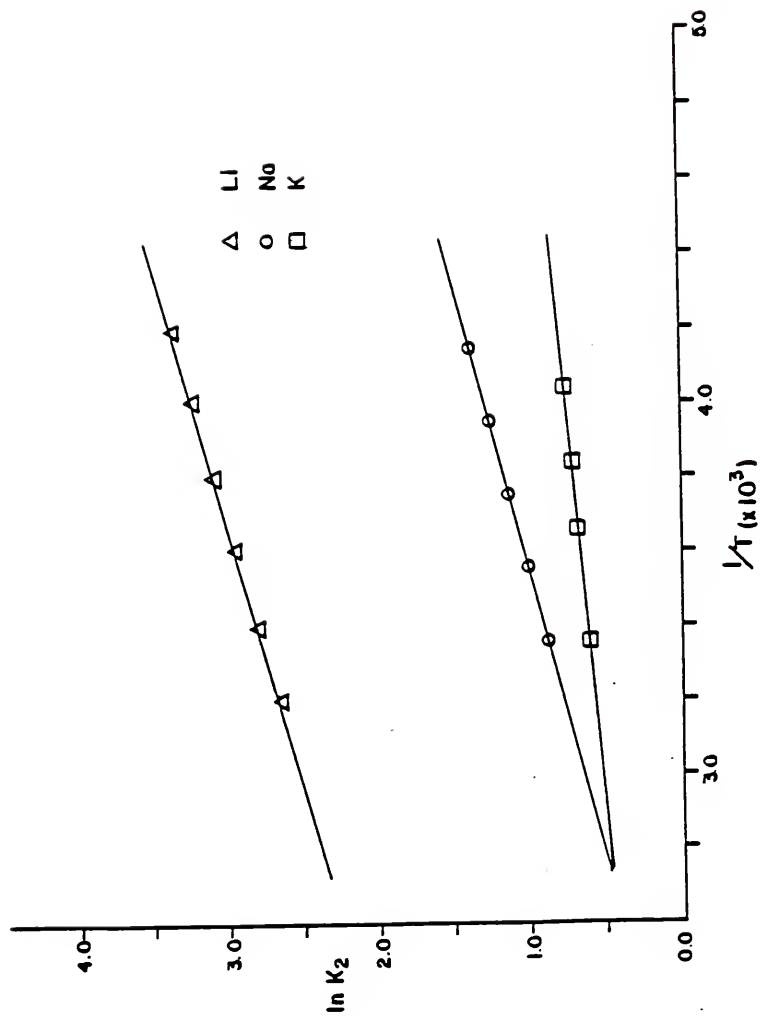
Figure 21. Plot of ln K_2 vs. 1/T for Dimer Anion [3] in Equation 4 with Various Counterions.

In an analogous study, Tsvetanov et al.[47] used IR spectroscopy to measure equilibrium constants for the coordination of the alkali metal in the active center of "living" oligo-isopropenyl methyl ketone by carbonyl groups on the oligomer chain (Equation 6). The values of K_2 for the corresponding lithio salts in THF were found to be about 5 at -30°C, compared with about 27 in the case of anion [3]. This is not unexpected in view of the greater coordinative ability of the 2-pyridyl group. Tsvetanov et al. also studied the effect of the number of monomer units in the chain on the apparent equilibrium constant and found an increase in K_2 as the degree of polymerization increased up to D.P. of 3 for Li^+. Attempts to study the effect of the chain length on K_{app} in our case led to the formation of side products complicating such studies. Side product formation will be dealt with in the next chapter.
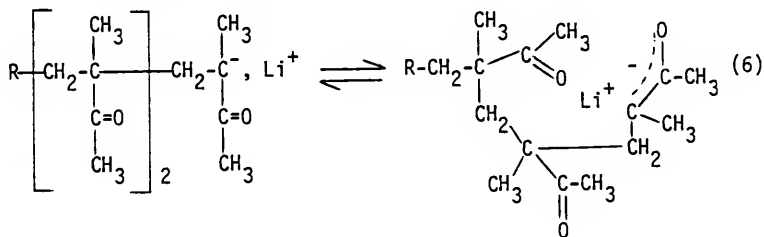
The ionic species in Equilibria 4 and 5 may exist in several forms, i.e., contact ion pairs, solvent-separated ion pairs, free ions, or ion-pair aggregates. If the ratios between two or more of these ionic species are different on each side of the equilibrium, this would profoundly affect the apparent equilibrium constant, making the correct determination of K_1 and K_2 impossible. Consider, for

example the equilibrium (7),

$$CH_3CHR^-,\ M^+ + CH_3CHRCH_2CH_2R \underset{\longleftarrow}{\overset{K_{ip}}{\longrightarrow}} CH_3CH_2R + CH_3CHRCH_2CHR^-,\ M^+$$

$$\Big\updownarrow Kd_1 \qquad\qquad\qquad\qquad\qquad\qquad \Big\updownarrow Kd_2 \qquad (7)$$

$$CH_3CHR^- + M^+ + CH_3CHRCH_2CH_2R \underset{\longleftarrow}{\overset{K_i}{\longrightarrow}} CH_3CH_2R + CH_3CHRCH_2CHR^- + M^+$$

R = 2-pyridyl
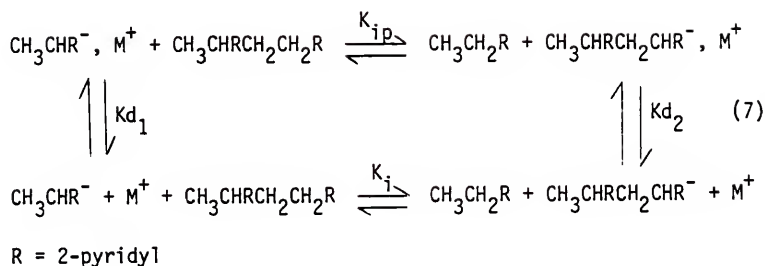
where a certain fraction of the ion pairs is dissociated into free ions. The overall equilibrium constant, K_{app}, may be shown to be[47]

$$K_{app} = K_{ip} \frac{(1-\alpha_1)}{(1-\alpha_2)} = K_i \left(\frac{\alpha_1}{\alpha_2}\right)$$

where α_1 and α_2 are the degrees of dissociation of the ion pairs CH_3CHR^-, M^+ and $CH_3CHRCH_2CHR^-$, M^+, respectively. Upon dilution, the equilibrium (7) will be expected to shift toward the salt with the largest dissociation constant. Similar expressions can also be derived for other concentration-dependent processes such as ion-pair aggregation.[48]

The lack of effect of concentration upon K_2 in Table 14 is clearly consistent with the view that ionization and other concentration-dependent processes such as aggregation are unimportant in the equilibrium. In support of this, conductometric and NMR measurements show that ionization of these 2-pyridyl substituted carbanions in THF is negligible ($K_d = 10^{-8}$ M).[7,12-14,49,50]

The fact that K_1 is greater than unity in the systems in which intramolecular coordination is not expected to be present indicates that some additional type of stabilization is present. This is perhaps due to a decrease in the dielectric constant of the medium in the vicinity of the ion pair caused by the presence of the penultimate group. For example, when the penultimate group is phenyl, no intramolecular cation coordination by a heteroatom is possible. However, K_{app} in this case is about 1.8 with Li^+, indicating that the phenyl group does play a role in stabilizing the ion pair. In addition, the lithium salt of [32] and the cryptated lithium salt of [3] yield K_{app} values which are also somewhat higher than unity. Since intramolecular coordination by penultimate pyridine nitrogen is expected to be disrupted in these systems, there appears to be a similar additional stabilization of the ion pairs. Thus, the values of K_2 reported in Table 14 should be interpreted as due to both intramolecular cation coordination by nitrogen and this small additional stabilizing effect.

CHAPTER VI

DEGRADATION REACTIONS OF OLIGOMER ANIONS

In studying the equilibria involving model trimers and tetramers (Equation 8), the presence of secondary reactions of the carbanions in

$$CH_3CHR^-, M^+ + CH_3(CHRCH_2)_nCH_2R \rightleftharpoons$$

[2]   [35], [36]   (8)

$$CH_3CH_2R + CH_3(CHRCH_2)_nCHR^-, M^+$$

[1]   [4], [5]

[35], [4] n = 2; [36], [5] n = 3; R = 2-pyridyl
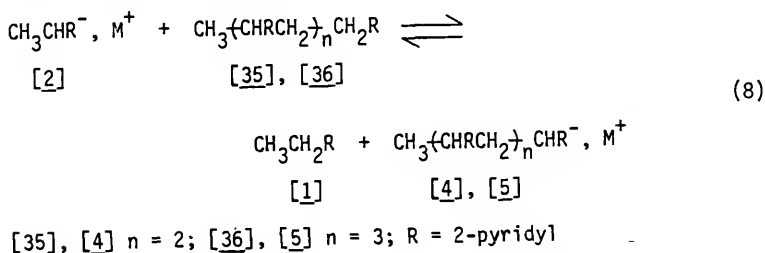
some cases complicated the determination of the equilibrium constants. This prompted an investigation of the pathways involved in the secondary reactions. Furthermore, a detailed analysis of the reaction products was expected to contribute to an understanding of the side reactions that accompany the corresponding polymerization reaction.

There are several types of secondary reactions conceivable in these systems. For example, it has been known for many years[51,52] that carbanions add to pyridine rings, and such reactions have been observed with poly-2-vinylpyridine.[53-57] Nucleophilic attack on the pyridine ring is also claimed during the initiation of the anionic polymerization of 2-vinylpyridine.[58,59] Another possible secondary reaction in Equation 8 is inter- or intramolecular abstraction of a

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methine proton on the backbone of the oligomer, leading to tertiary carbanions [37].

$$H(CH_2CHRCH_2)_n^- \overset{M^+}{\underset{}{C}}R(CH_2CHR)_m^-H$$

R = 2-pyridyl

m ≥ 1

n = 0, 1, 2

[37]
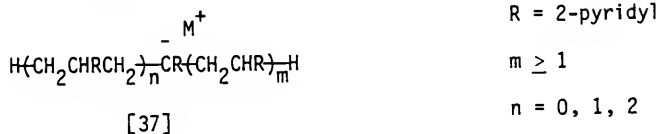
When the lithium or potassium salts of [2] were reacted with dimer [15] (Equation 9), side product formation occurred at a slow

$$CH_3CHR^-, M^+ \quad + \quad CH_3CHRCH_2CH_2R$$

[2]   [15]

R = 2-pyridyl

THF

(9)

CH_3OH ← → CH_3I

[1] + [6] +   [1] + [6] +

[15] + [39]   [38] + [40] + [15]
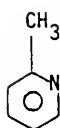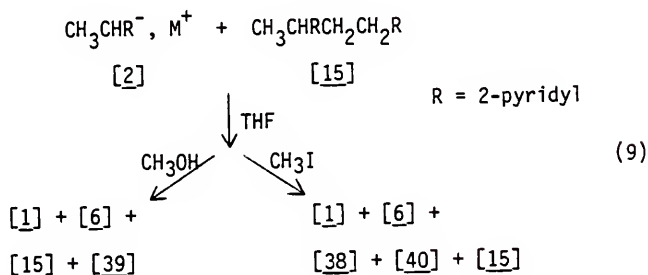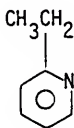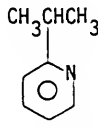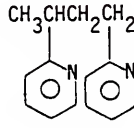
[39]   [1]   [40]   [15]
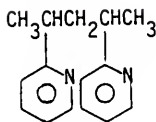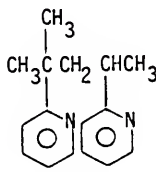
[6]   [38]

rate and did not interfere with the determination of the equilibrium constants. The fraction of side products remained negligible for

several hours at room temperature, whereas the proton transfer equi-
librium (Equation 4) was attained in about one hour. Table 16 lists
the products formed under various conditions as determined by LC sep-
aration followed by NMR and GC analysis. The side product obtained
upon methylation was 2-methyl-2,4-di(2-pyridyl)pentane [38]. 2-Methyl-
pyridine [39] and 2,4-di(2-pyridyl)pentane [6] were the side products
formed upon protonation with methanol.

Table 16

Product Fractions in Equation 9

| | | | | | | Product Fractions | | | |
| | | | | | Monomeric | | | Dimeric | |
M^+	Electro- phile	T(°C)	Time (hrs)	[39]	[1]	[40]	[15]	[6]	[38]
Li	CH_3OH	25	168	0.06	0.50	-	0.20	0.24	-
Li	CH_3I	25	168	-	0.30	0.35	-	0.16	0.20
Li	CH_3I	0	150	-	0.33	0.06	0.07	0.47	0.06
Li	CH_3I	-25	94	-	0.26	0.06	0.05	0.61	0.03
Li	CH_3I	-25	150	-	0.30	0.05	0.08	0.56	0.02
K	CH_3I	25	92	-	0.27	0.19	0.04	0.37	0.13
K	CH_3I	0	92	-	0.29	0.21	0.10	0.31	0.09
K	CH_3I	-25	94	-	0.28	0.24	0.08	0.36	0.04
K	CH_3I	-78	94	-	0.15	0.36	0.19	0.25	0.05

Alkali metal salts of 2-ethylpyridine [2] were also reacted with
tetramer [36] followed by alkylation or protonation (Equation 10).
The reaction products were separated by LC and identified by NMR and

$$CH_3CHR^-, M^+ \quad + \quad CH_3(CHRCH_2)_3CH_2R$$

$$[\underline{2}] \hspace{4cm} [\underline{36}]$$

$$\Big\downarrow \text{ THF}$$

$$CH_3CH_2I \diagup \quad \diagdown CH_3OH \hspace{3cm} (10)$$

Left branch:

$$CH_3(CHRCH_2)_nCH_2R$$

$$[\underline{1}], [\underline{15}], [\underline{35}], [\underline{36}]$$

$$+ \ CH_3(CHRCH_2)_nCHRC_2H_5$$

$$[\underline{41}] - [\underline{44}]$$

Right branch:

$$[\underline{1}], [\underline{15}], [\underline{35}], [\underline{36}]$$

$$+ \ CH_3(CHRCH_2)_nCHRCH_3$$

$$[\underline{6}], [\underline{7}]$$

$$+ \ H(CHRCH_2)_nCH_2R$$

$$[\underline{45}], [\underline{46}]$$

$$R = 2\text{-pyridyl}$$

$$[\underline{36}], [\underline{44}] \ n = 3$$
$$[\underline{7}], [\underline{35}], [\underline{43}], [\underline{46}] \ n = 2$$
$$[\underline{6}], [\underline{15}], [\underline{42}], [\underline{45}] \ n = 1$$
$$[\underline{1}], [\underline{41}] \ n = 0$$
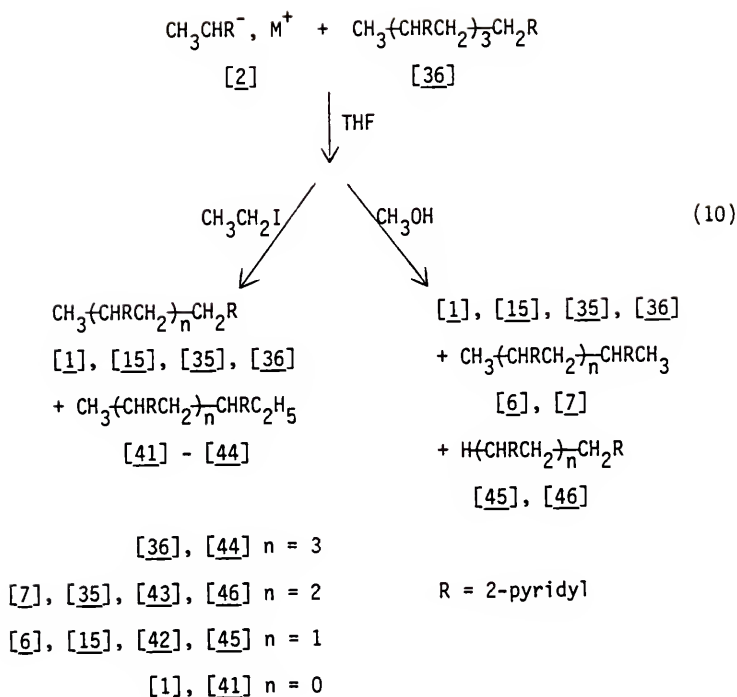
GC analysis. It appears that most of the tetramer was cleaved to dimer and trimer within 2 hours at room temperature (Table 17). In accord with this, other workers have observed a decrease in molecular mass of poly-2-vinylpyridine when treated with polystyryl anions[54-56] or cumyl potassium.[55]

Scheme 2 shows a mechanism which is consistent with the types of side products formed in Equations 9 and 10. Initially, formation of a carbanion on the backbone of the oligomer occurs by inter- or intra-molecular abstraction of a methine proton. The chain may then cleave by an elimination reaction yielding an alpha substituted vinylpyridine

Table 17

Product Fractions in Equation 10^{a,b}

Run	M$^+$	T(°C)	Reaction Time	Electrophile	Tetramer			Unidentified [X]	Trimer				Unidentified [X]
					[36]	[8]	[44]		[35]	[7]	[43]	[46]	
(1)	Li	25	2 hrs	CH$_3$CH$_2$I	0.11	-	0.05	0.02	0.01	-	0.07	-	0.02
(2)	Li	25	3.5 hrs	CH$_3$CH$_2$I	0.01	-	0.01	0.01	0.02	-	0.06	-	0.03
(3)	Li	25	6 hrs	CH$_3$CH$_2$I	0.01	-	0.01	0.01	0.02	-	0.05	-	0.04
(4)	Li	0	16 hrs	CH$_3$CH$_2$I	0.19	-	0.47	0.03	0.01	-	0.12	-	0.02
(5)	K	25	1.5 hrs	CH$_3$OH	0.66	-	-	0.09	0.05	0.02	-	0.02	0.05

Run	Dimer				Unidentified [X]	Monomer	
	[15]	[6]	[42]	[45]		[1]	[41]
(1)	0.12	-	0.52	-	0.06	0.06	0.08
(2)	0.07	-	0.60	0.01	0.09	0.09	0.02
(3)	0.10	-	0.56	0.01	0.12	0.08	0.02
(4)	0.01	-	0.25	-	0.03	0.17	0.06
(5)	0.10	0.01	-	0.02	-	-	-

a Products identified by LC isolation and NMR analysis along with comparison of GC retention times to model compounds.

b Unidentified products were present in small amounts and could not be isolated by LC. Their GC retention times did not correspond to any model oligomer compound previously synthesized.

Scheme 2

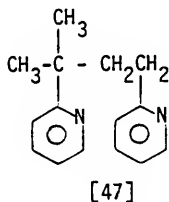[15] [48]

[3] [2]

[7] or

[6] or [38]

[49]

[50]
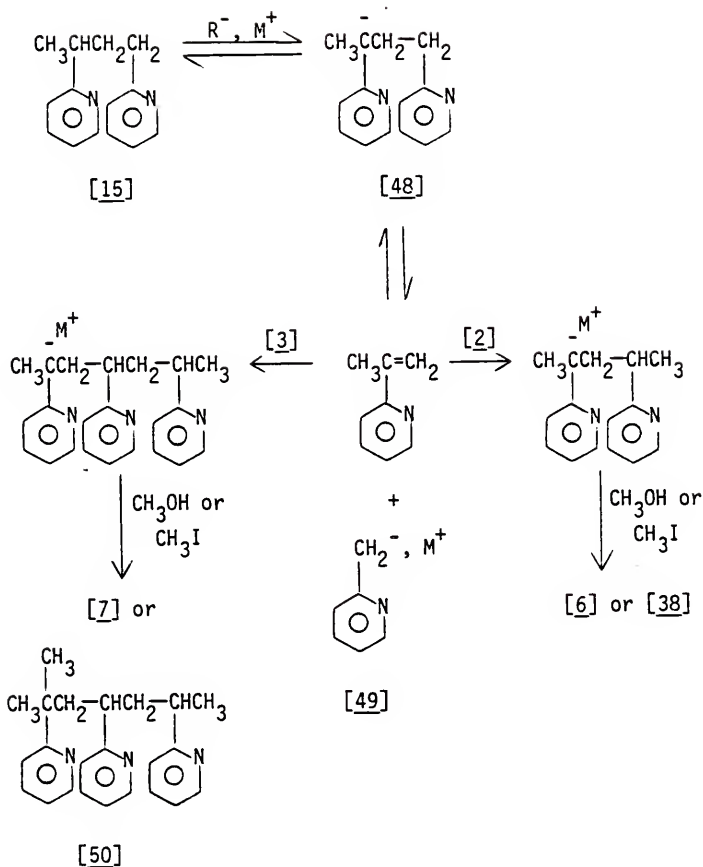
and a new carbanion. This elimination may proceed in either a con-
certed (E2) or stepwise (Elcb) fashion. The concentration of these
vinylpyridines would be expected to remain very low due to their sub-
sequent reaction with carbanions. An overall decrease in the average
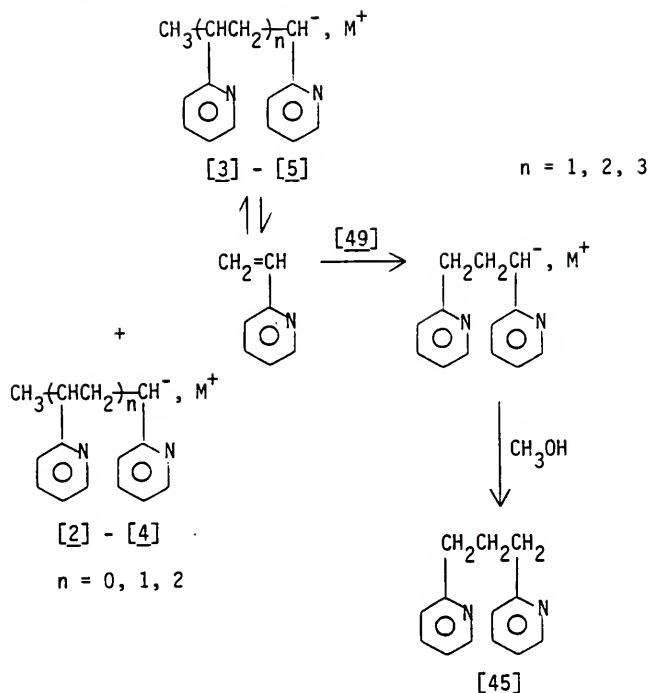molecular weight of the oligomers will be realized if the vinylpyridine

combines with an anion which is smaller than the cleaved anion fragment. This is a very likely occurrence, since the 2-ethylpyridyl anions [2] are present in large quantity in the solution. Consistent with the proposed mechanism, small amounts (~1%) of trimeric and tetrameric products are also formed, presumably by addition of dimer anion [3] to the vinylpyridine produced upon cleavage (Equation 9). In addition, this mechanism predicts that oligomers [6] and [7] will be formed upon protonation (Scheme 2), and this is consistent with the observed results.

Elimination may also occur from the secondary carbanions [3] - [5], yielding a carbanion and 2-vinylpyridine (Scheme 3). Small amounts of oligomers [45] and [46] are observed in the product mixtures (Table 17), indicating the participation of this pathway.

It is interesting to note that essentially no 3-methyl-1,3-di-(2-pyridyl)butane [47] is formed upon methylation in Equation 9. This result is somewhat puzzling since the formation of this product would be predicted by Scheme 2. The absence of [47] may be due to the fact that the intermediate anion [48] would form very slowly as described in Chapter 5. The subsequent elimination reaction may now occur rapidly, thus keeping the concentration of anion [48] very low at all times.

$$
\begin{array}{c}
CH_3 \\
| \\
CH_3-C \ - \ CH_2CH_2 \\
| \\
\end{array}
$$

[47]

Scheme 3

$$CH_3(CHCH_2)_nCH^-, M^+$$

[3] - [5]   n = 1, 2, 3

$$\xrightarrow{[49]}$$

$$CH_2=CH$$ $$CH_2CH_2CH^-, M^+$$

+

$$CH_3(CHCH_2)_nCH^-, M^+$$

[2] - [4]

n = 0, 1, 2

$$CH_3OH$$

$$CH_2CH_2CH_2$$

[45]

An important factor in the cleavage of the oligomer chains by an elimination mechanism is the ability of an α-pyridyl carbanion to act as a leaving group. Negatively charged carbon species are generally considered extremely poor leaving groups in alkene-forming elimina-tions,[60] but such reactions have been reported.[61] Carbanions as leav-ing groups are quite common, however, in carbonyl-forming eliminations such as reverse aldol, Claisen, and Michael reactions.[61] Examples involving α-pyridyl carbanions as leaving groups in an elimination reaction include the anionic depolymerization of poly-2-vinylpyridine[62]

and poly-2-isopropenyl pyridine[63] which occurs at high temperatures (Equation 11). In the depolymerization, monomer is eliminated from the living chain end resulting in the formation of a new carbanion site.


$$R = CH_3, H$$
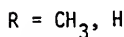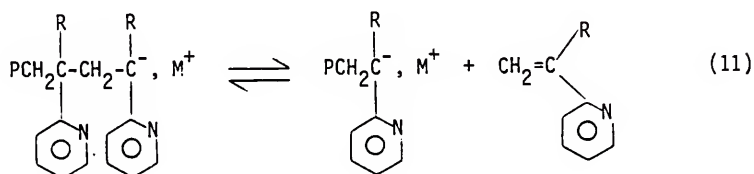
Another mechanism which could explain the observed chain cleavage involves the nucleophilic attack of an α-pyridyl carbanion on a methyl or methylene carbon of the oligomer followed by displacement of another α-pyridyl carbanion (Scheme 4). This scheme is less likely for

Scheme 4
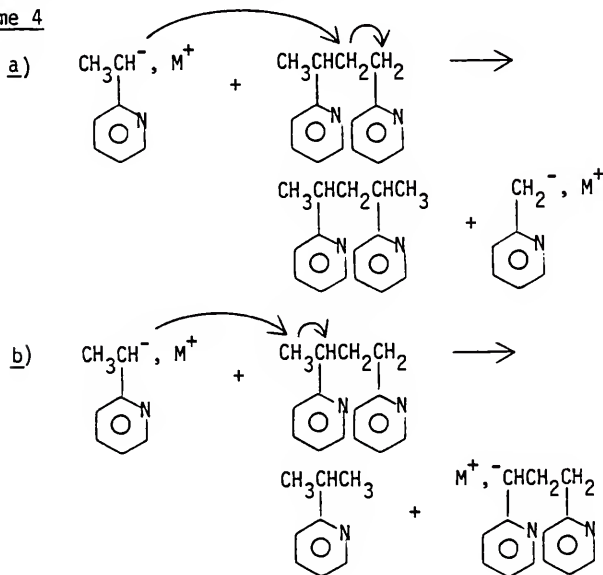
the following reasons. First, no 2-isopropylpyridine [40] was pro-
duced upon protonation (Equation 9 or 10) as would be expected by
this mechanism (Scheme 4b). Second, a mixture of lithio-2-ethylpyri-
dine [2] and 2-ethylpyridine in THF also failed to produce 2-isopro-
pylpyridine after 6 days at room temperature. Third, no 2-phenyl-4-
(2-pyridyl)pentane [51] was observed in the reaction of dimer [31]
with the lithium or potassium salts of [2] (Equation 12). Dimer [51]

$$\text{(12)}$$

[2]   [31]   [1]   [51]
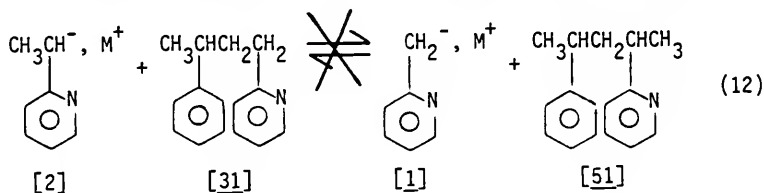
would be expected to form if nucleophilic substitution occurs at the
methylene group but would not likely occur from an elimination process
followed by addition of a carbanion (Equation 13). The intermediate
carbanion [52] would not be expected to form, since the α-pyridyl pro-
tons are at least 5 pKa units more acidic than the benzylic proton.

[52]

$$\text{(13)}$$

[2]

[51]
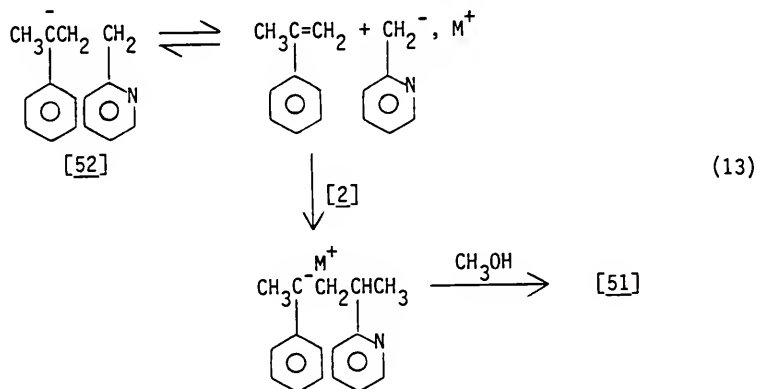
Further evidence against a nucleophilic substitution mechanism in the cleavage of oligomers is given by examination of the products obtained by protonation of the equilibrium reaction shown in Equation 14. In addition to [1] and [47], substantial amounts of [6], [15],
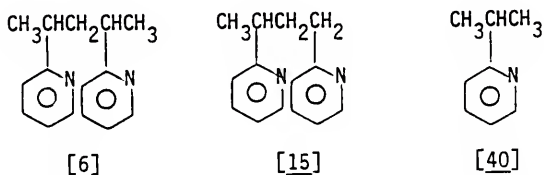
$$(CH_3)_2CCH_2-CH_2 + CH_3CH^-, Li^+ \xrightarrow[\text{51 hrs.}]{\overset{25°C}{\rightarrow}}_{\text{THF}}$$

[47]   [2]   (14)

$$(CH_3)_2CCH_2-CH^-, Li^+ + CH_3CH_2$$

.[1]
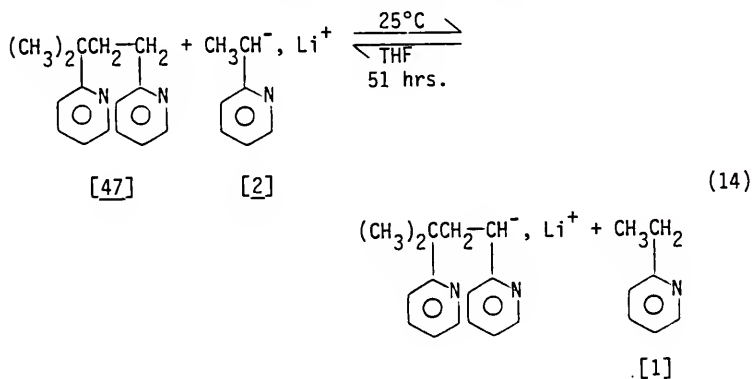
and [40] are formed. All of these products could be produced by either a substitution or an elimination mechanism (Schemes 5 and 6), but a substitution reaction would also produce 2-methylpyridine [39]

$$CH_3CHCH_2CHCH_3 \qquad CH_3CHCH_2CH_2 \qquad CH_3CHCH_3$$

[6]   [15]   [40]

and 2-methyl-2,4-di-(2-pyridyl)pentane [38]. The observed lack of these two products is consistent with an elimination mechanism.

It is interesting to note that no side products were obtained which resulted from attack of an α-pyridyl carbanion on the pyridyl rings of the oligomers. This is consistent with the fact that side

Scheme 5

$(CH_3)_2CCH_2CH^-$, M^+ ⇌ $(CH_3)_2C^-$, M^+ + $CH_2=CH$

↓ CH_3OH ↓ [2]

CH_3CHCH_3 [40]

$CH_3CHCH_2CH^-$, M^+

↓ CH_3OH

$CH_3CHCH_2CH_2$ [15]

$CH_3C-CH_2CH_2$ ←R^-, M^+←

M^+

CH_2^- M^+ + $CH_3C=CH_2$

↓ [2]

CH_3C CH_2CHCH_3 →CH_3OH→ $CH_3CHCH_2CHCH_3$ [6]

Scheme 6

CH_3CH^-, M^+ + $(CH_3)_2CCH_2CH_2$ $\longrightarrow$ $(CH_3)_2C^-M^+$ + $CH_3CHCH_2CH_2$

[15]

$(CH_3)_2C\ CH_2CHCH_3$

[38]

+

CH_2^-, M^+

$\downarrow$ CH₃OH

CH_3

[39]

$\downarrow$ CH₃OH

CH_3CHCH_3

[40]

$\downarrow$ [2]

$CH_3CHCH_2CHCH_3$

[6]

+

CH_2^-, M^+

CH₃OH
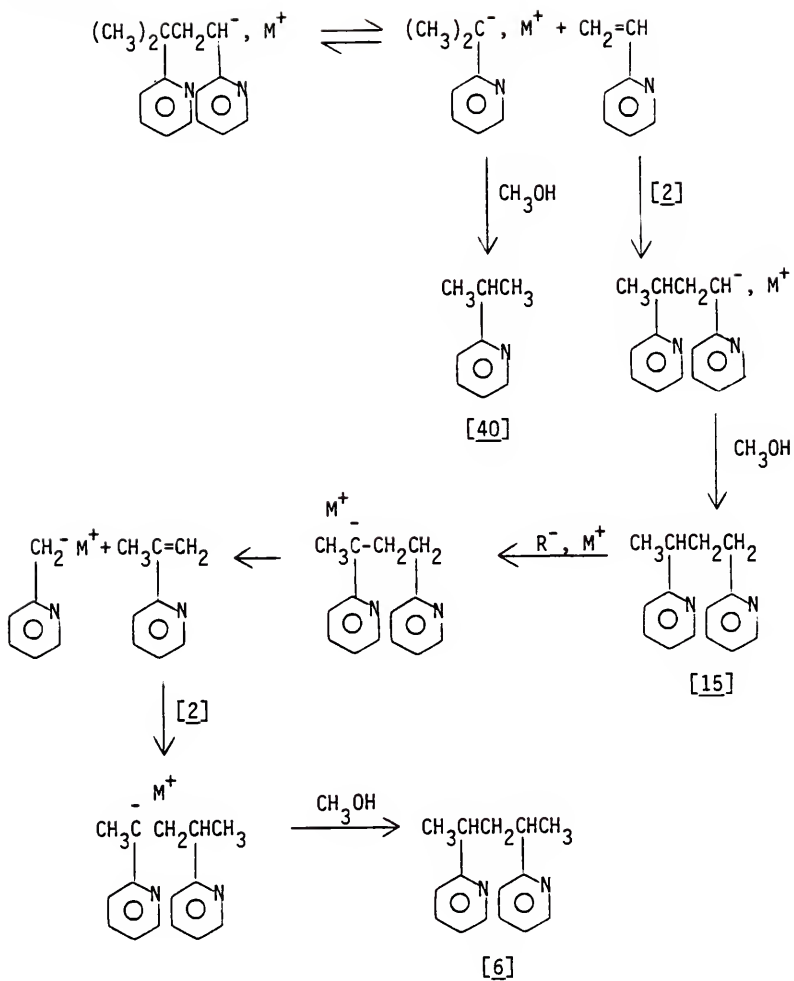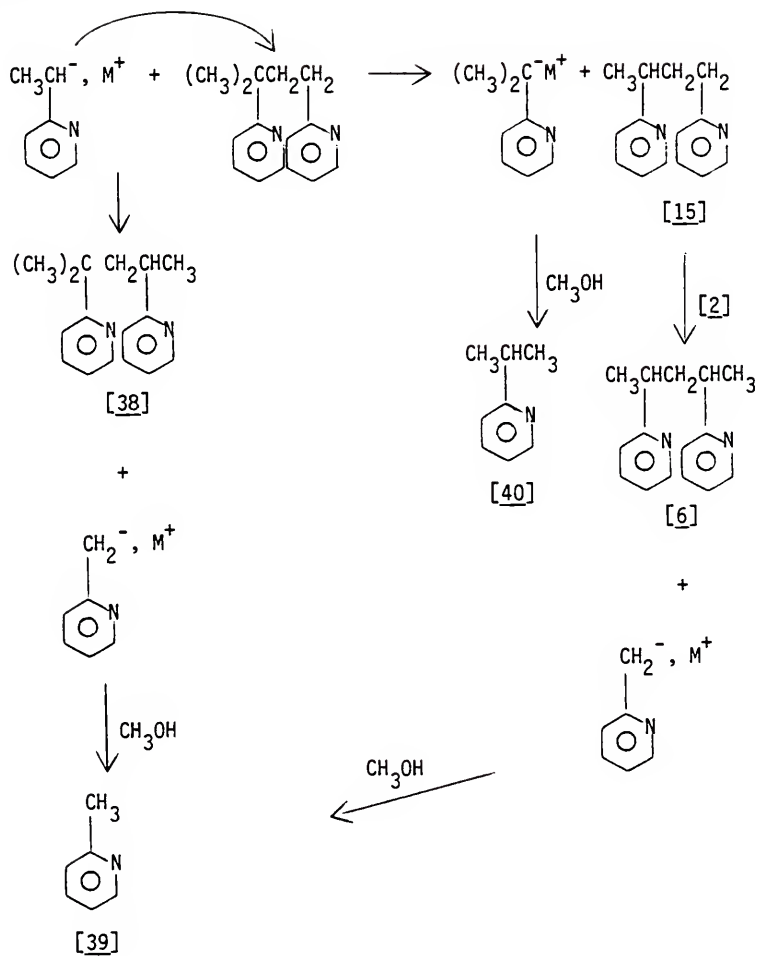
products were never formed in mixtures of 2-ethylpyridine and lithio-2-ethylpyridine. Nucleophilic attack on the pyridine rings of poly-2-ethylpyridine has been previously postulated[53-57] with such species as Grignard reagents, butyllithium, and polystyryl anions. These species are generally more nucleophilic than α-pyridyl carbanions, which may account for the lack of ring attack in the latter case.

In some cases, an increase in the $\overline{M}_w$ of the polymer,[57] gel formation,[56] or cross-linking[64] has been observed upon treatment of poly-2-vinylpyridine with carbanions. Scheme 7 illustrates how this type of phenomenon may also be consistent with the proposed mechanism. Cleavage of the polymer chain (pathway a) leads to the formation of a polymer with a terminal double bond which may be considered a "macro-mer". The reaction of a "macromer" with a carbanion on another poly-mer chain leads to branching (pathway b). When a terminal double bond on a branched polymer reacts with a carbanion on a polymer back-bone, cross-linking may occur (pathway c). Stannett et al.[56] have proposed a mechanism for gel formation in which a living poly-2-vinyl-pyridine chain attacks a pyridine ring on another poly-2-vinylpyridine chain. This does not seem very likely since there appears to be no nucleophilic attack on the pyridine rings of dimer, trimer, and tet-ramer of 2-vinylpyridine by α-pyridyl carbanions.

In conclusion, by using oligomeric model compounds, it has been shown that carbanions may cleave poly-2-vinylpyridine chains probably by means of an elimination mechanism that involves abstraction of an α-pyridyl proton on the polymer backbone. In some cases, branching or cross-linking may occur by this mechanism. With α-pyridyl carbanions,

Scheme 7
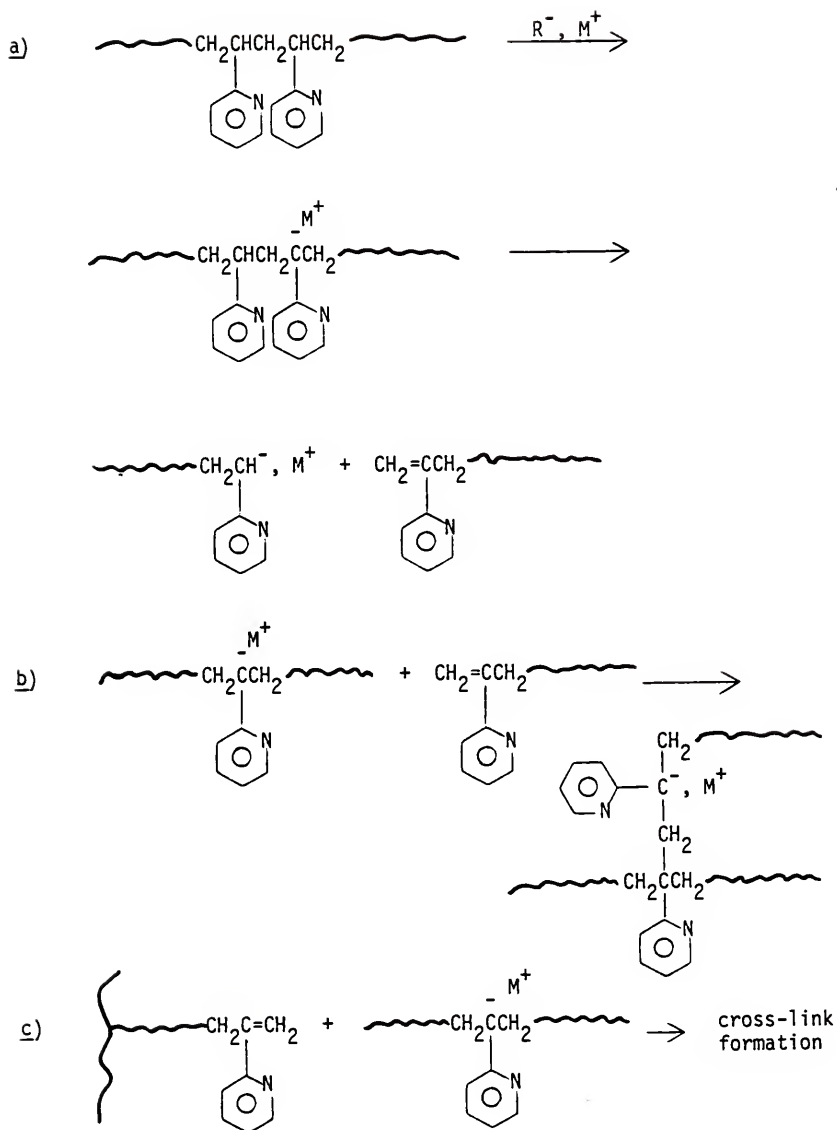
no nucleophilic addition appears to occur on the pyridine rings of the polymer, but with a more nucleophilic species such as polystyryl-lithium this seems to be a likely possibility. Except for lack of attack on the pyridine rings, our results are in good agreement with the mechanism proposed by Fontanille and Sigwalt[55] for cleavage of poly-2-vinylpyridine chains by carbanions.

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BIOGRAPHICAL SKETCH

Craig C. Meverden was born May 15, 1956 in Rockford, Illinois. After graduation from Rockford Jefferson High School in 1974, he attended Illinois State University, where he received a B.S. degree in chemistry in 1978.
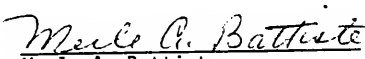
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In 1979, he married Paula Jane Bailey.

I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

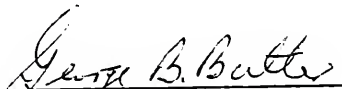Thieo E. Hogen-Esch, Chairman
Professor of Chemistry

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August, 1983

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